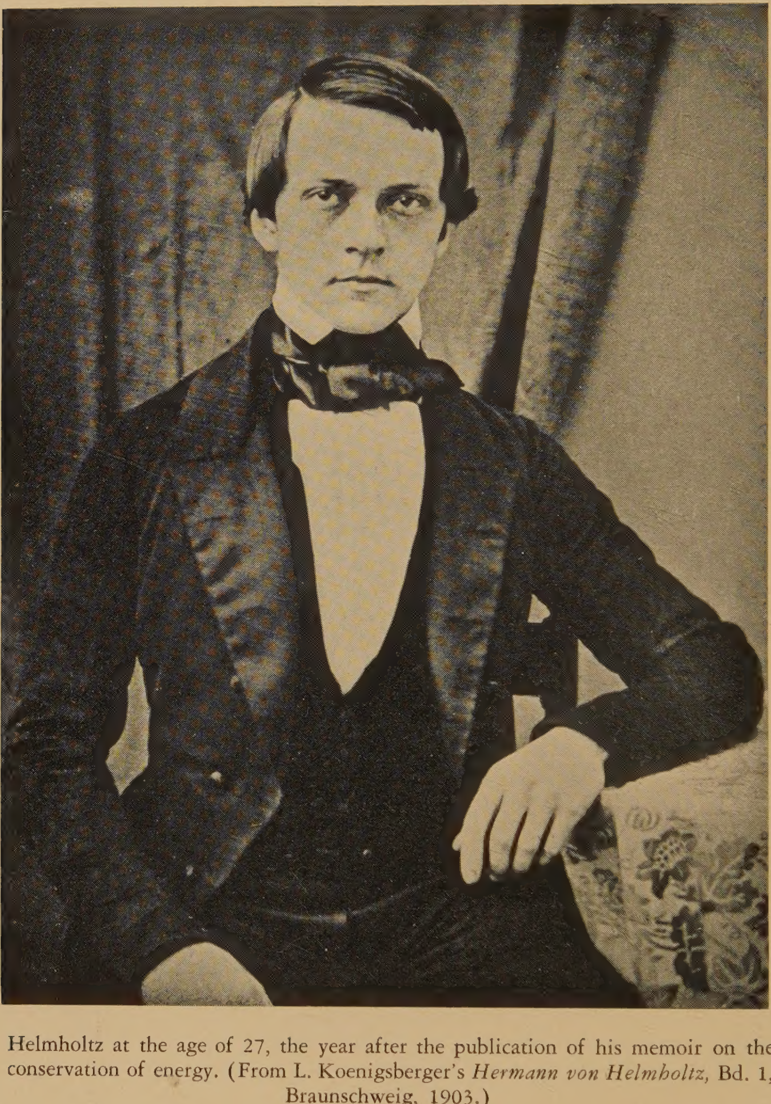
Maude Williams

1930

EX LIBRIS
ROBERT L. PHILLIPS, M.D.

SELECTED READINGS
IN THE HISTORY OF
PHYSIOLOGY



Helmholtz at the age of 27, the year after the publication of his memoir on the conservation of energy. (From L. Koenigsberger's *Hermann von Helmholtz,* Bd. 1, Braunschweig, 1903.)

SELECTED READINGS IN THE HISTORY OF PHYSIOLOGY

Edited by

John Farquhar Fulton, M.D.
Formerly Fellow of Magdalen College, Oxford.
Sterling Professor of Physiology,
Yale University

CHARLES C THOMAS · PUBLISHER
SPRINGFIELD · ILLINOIS BALTIMORE · MARYLAND
MDCCCCXXX

COPYRIGHT, 1930, BY CHARLES C. THOMAS

MADE IN THE UNITED STATES

TO

L. P. F.

EVERY good thing is known and defined by its best, and it is from moments such as those, which happen in all the arts, that we may know what art is and why it is valued. All excellence is rare and hard, and the greatest artists seldom achieve that which, finally, art exists to achieve. Poets are always writing, painters painting, musicians composing, in the hope that this, which they cannot will, may happen to them. They spend a vast deal of energy on their work, much of which seems wasted in sentiment or pedantry or the solution of some technical problem; but men choose art for the business of their lives, and labour at it alone and without pudding or praise, for the sake of these moments which have happened to other artists and may happen to them. And the world with all its indifference to art yet does value these moments and preserves with a religious awe the works in which they occur. The value is half unconscious, the awe seldom expressed; but all human beings think better of humanity because Shakespeare and Beethoven and Michelangelo were men and had the power of saying more than mortal things. A. Clutton-Brock, *Essays on Literature & Life* ("Pure Literature").

PREFACE

LONG'S attractive *Readings in pathology*[1] which was published in 1929, suggested to me that a similar volume of physiological readings might prove acceptable. My qualifications for editing such a work are meagre enough, but the problem of selection was to some extent simplified by having at hand many of the necessary texts. For several years I have collected books relating to the history of physiology, and at odd times I have tried to follow Osler's practice of placing slips beside passages which have exerted a great influence upon the development of physiological thought. Such passages—especially those which describe an important discovery—have a peculiar fascination for many people, and they often prove a great stimulus to those who are entering upon the study of science. In many places where physiology is taught, contact with the original sources is necessarily infrequent, and a pupil's outlook tends to be confined to second-hand knowledge obtained from lectures and text-books. For many reasons it is desirable that a medical student be conducted early in his career to the front line trenches of medical and physiological discovery. Let him realize that men as young as himself have made important contributions: that de Graaf at 23 years of age devised the first pancreatic fistula; that Helmholtz at 24 measured for the first time the heat production of frog muscle; that Johannes Müller at 25 had enunciated the principle of specific nerve energies. Let him discover that simple facts were once hidden in a fog of faulty observation and faulty reasoning, and that it was sometimes the enquiring minds of students like himself that made matters clear.

In order to preserve the sequence of ideas in the several fields of physiological thought, the material in this volume has been grouped in subjects:—*e.g.,* circulation, respiration, digestion, etc., each group arranged in chronological order. It must not be supposed, however, that such a collection of annotated readings represents in any sense a history of physiology; it is intended rather to resemble the 'source book' of the professional historian, and as such cannot be expected to tell the continuous story of a given subject or period.

---

[1] Long, E. R. *Selected readings in pathology from Hippocrates to Virchow.* Springfield, Illinois: Baltimore, Maryland: Charles C. Thomas, xiv+301 pp., 4 leaves, 1929.

I shall not attempt here to justify my choice of readings; the reason for the inclusion of Lavoisier's discovery of oxygen, is self-evident; with others a personal bias may have determined the choice, but this, I suppose, is inevitable. Occasionally an author is 'represented' because he exerted a great influence on physiology, though his discoveries may have been of little importance (*e.g.,* Haller). In a few instances selections are included from writers who preached doctrines found later to be false. Fabricius and Alexander Walker, though wrong, are more interesting than many who have been right; and to anyone who concerns himself with the psychology of discovery, Fabricius's book on the valves in the veins is one of the most remarkable documents in scientific history,—deserving incidentally to be reprinted in facsimile with translation. It is interesting primarily because it was wrong: he had accurately assembled the essential facts, the circulation lay before him, and yet he did not see it. Why did he fail? Probably for much the same reason that we fail now to make the great discoveries of to-morrow: the scientific background was absent which would have given him the aptitude to see. It is a curious and important fact that though Fabricius did not himself grasp the circulation, he undoubtedly sowed in the mind of his young English pupil the seeds that came to such rich fruition.

In dealing with modern literature it is often difficult to assign credit for a given discovery, and still more difficult to choose the passage which contains the description of an important contribution. Teamwork, healthy interchange of ideas between investigators, and many other factors associated with modern scientific work combine to prevent final judgment of priority. Similar difficulty is evidently experienced by the Nobel Committee if we may judge from the frequency in recent awards that the prize has been divided between two individuals working in the same field. Who, for example, was responsible for the discovery of the true nature of mountain sickness, or of the volume output of the heart? Coming to the endocrines the uncertainty, except for the paper of Oliver and Schafer, is even greater, and in consequence I have made but few selections in this and similar fields in which I did not feel competent to pass judgment.

After the material had been collected several facts of interest emerged. Of the 65 selections of which information was available concerning the age of the author when the work was done, 11 were written between 20 and 30 years of age,—Mayow and de Graaf being 23, Arrhenius 24, and Helmholtz (Conservation of Energy), Blagden, Cannon and

Herbert Mayo 26; 23 were written between the ages of 30 and 40 years, and the remaining 42 were written when their authors were over forty. De Réamur, for example, was actually 69 when he carried out his memorable observations upon the digestive juice of his pet kite.

The frequency with which far-reaching conclusions have been drawn from experiments upon human beings deserves also to be mentioned. I was unaware of this when starting to make the selections, and if asked beforehand I should have replied that, with a few notable exceptions, such as Beaumont's observations, the chief advances in physiology had come from animal experimentation, where conditions can usually be more readily controlled than in man. However, I find that 14 of the 85 selections were based chiefly, if not entirely, upon human experimentation. One need only mention Sanctorius, Fabricius, Spallanzani, Blagden, Beaumont, Haldane and Priestley, Barcroft, Cushing, and Lewis, all of whom obtained evidence which would have been either impossible, or far less convincing had the observations been carried out upon animals. This should prove a great stimulus to those who have at their disposal extensive clinical resources.

Some passages present a peculiar appeal from the light which they shed upon the personality of the writers.[2] Who has not smiled over Malpighi's confession that in studying the capillary circulation he had "destroyed nearly the whole race of frogs—which," he adds, "does not happen in that savage batrachomyomachia of Homer"; or, in reading Boyle's crucial experiment upon the volume and pressure of gases, who has not experienced the feeling of delight that Boyle himself displayed as he wrote. Such details make science vivid and real, and they give human interest to facts which might otherwise seem dull and irrelevant. And they serve to remind us that, no matter how much science may advance, personality will always be a living force in Medicine, not only at the bedside, but also in the laboratory. How well was this illustrated by the life and influence of William Osler! He had a touch of St. Francis about him and there will always be room in Medicine for men of his genius.

---

[2] This is illustrated in another way in Sir William Osler's catalogue in which the great characters of medical history are made to live again by virtue of the personal detail which Osler skilfully included in his attractive annotations. *Bibliotheca Osleriana. A catalogue of books illustrating the history of medicine and science collected, arranged, and annotated by Sir William Osler, Bt. and bequeathed to McGill University.* Oxford: at the Clarendon Press, xxxv+786 pp., 1929 [Edited by W. W. Francis, R. H. Hill and Archibald Malloch with the assistance of L. L. Mackall, R. R. Trotman and others].

The transcriptions have been made from the earliest editions of a work and in the foot-notes full bibliographical description is given of each book or journal cited, with the pagination of the quotation itself (in parenthesis). Care has been taken to preserve original spelling and punctuation of all English passages. Selections originally in French, German or Latin have been given, where possible, in contemporary English translation. When no translations exist or when those available have seemed inaccurate, the passage has been rendered into modern English. In translations from French, my labours have been considerably lightened by my secretary, Miss Holmes, who is an accomplished French scholar; in translating from Latin, I have had the invaluable assistance of my friend, Arnold Meadowcroft Muirhead, M.A., formerly of Brasenose College, who has given most generously of his time. For the final form of all translations, however, and for technical phraseology, I must hold myself personally responsible. Except in two instances I have avoided the use of Sir Michael Foster's excellent translations already available to physiologists in his *Lectures on the history of physiology.*

The illustrations have been selected without any special criterion of suitability except personal preference and the desire not to repeat the figures and portraits so often seen in other historical works on physiology. The frontispiece of Helmholtz, made from a daguerreotype taken at the age of 27 (1848), the year after the publication of his memoir on the conservation of energy will, it is hoped, not be deemed inappropriate; for I am in sympathy with those who feel that this gifted man possessed one of the most remarkable intellects that ever applied itself to physiological thought.

* * * * *

I should like to take this opportunity of expressing my sincere thanks to the Publisher, whose resourcefulness and judgment will be evident to the reader of these pages. He has identified himself with physiology, ancient and modern, and one hopes that we shall long continue to have the benefit of this enthusiastic cooperation.

J. F. FULTON

Magdalen College,
Oxford. April 8, 1930.

CONTENTS

DEDICATION v
PREFACE vii
ILLUSTRATIONS xvii

Chapter I: GENERAL PRINCIPLES

JEAN REY (1575-1645)
"On the reason why tin and lead increase in weight on calcination," 1630 4
ROBERT BOYLE (1627-1692)
"Defence of the Doctrine touching the Air," 1662 6
CHARLES BLAGDEN (1748-1820)
"Experiments and Observations in an heated room," 1775 11
ROBERT BROWN (1773-1858)
"On the particles contained in the pollen of plants," 1828 15
HERMANN VON HELMHOLTZ (1821-1894)
"On the conservation of energy," 1847 18
JAKOBUS HENRICUS VAN'T HOFF (1852-1911)
"The rôle of osmotic pressure in the analogy between solutions and gases," 1887 22
SVANTE ARRHENIUS (1859-1927)
"On the dissociation of substances in aqueous solution," 1887 . . . 23
ERNEST HENRY STARLING (1866-1927)
"Absorption by blood vessels," 1895 26
JOHN SCOTT HALDANE
"Preface of his *Respiration,* 1922 31
LAWRENCE JOSEPH HENDERSON
"The fitness of the environment," 1913 33

Chapter II: THE CIRCULATION OF THE BLOOD

ARISTOTLE (384-322 B.C.)
"De partibus animalium," 38
GALEN (131-201 A.D.)
"De usu partium" 41
MICHAEL SERVETUS (1509-1553)
"Christianismi restitutio," 1553 43
HIERONYMUS FABRICIUS AB AQUAPENDENTE (1537-1619)
"De venarum ostiolis," 1603 47

WILLIAM HARVEY (1578-1657)
"Exercitatio anatomica de motu cordis et sanguinis in animalibus," 1628 50
STEPHEN HALES (1677-1761)
"Statical essays: containing hæmastaticks; or an account of some hydraulick and hydrostatical experiments made on the blood and blood-vessels of animals," 1733 57

Chapter III: THE CAPILLARIES

MARCELLO MALPIGHI (1628-1694)
"De pulmonibus Observationes anatomicæ," 1661 61
ANTONY VAN LEEUWENHOEK (1632-1723)
"On capillary circulation in frogs," 1688 68
STEPHEN HALES (1677-1761)
"Statical essays: containing hæmastaticks; or an account of some hydraulick and hydrostatical experiments made on the blood and blood-vessels of animals," 1733 75
ROBERT WHYTT (1714-1766)
"An inquiry into the causes which promote the circulation of the fluids in very small vessels of animals," 1755 79
ALBRECHT VON HALLER (1708-1777)
"On the movement of the blood and the effects of bleeding," 1756 . 82
JOHANNES MÜLLER (1801-1858)
"On the contractility of the capillaries," 1838 86
ALEXANDER PHILIP WILSON PHILIP (circa 1770-1851?)
"An experimental inquiry into the laws of the vital functions," 1826 88
JAMES BLACK (1788-1867)
"A short inquiry into the capillary circulation of the blood," 1825 . 91
CHARLES-MARIE-BENJAMIN ROUGET (1824-1904)
"On the contractility of blood capillaries," 1874 and 1879 . . . 94
SCHACK AUGUST STEENBERG KROGH
"The anatomy and physiology of capillaries," 1922 100
THOMAS LEWIS
"The blood vessels of the human skin and their responses," 1927 . 103

Chapter IV: RESPIRATION

ROBERT BOYLE (1627-1692)
"On respiration," 1660 107
ROBERT HOOKE (1635-1703)
"Of preserving animals alive," 1667 109
JOHN MAYOW (1645-1679)
"On respiration," 1668 111

RICHARD LOWER (1631-1691)
"On pulmonary circulation," 1669 116
JOSEPH PRIESTLEY (1733-1804)
"Experiments and observations on different kinds of air," 1774-1777 . 119
ANTOINE-LAURENT LAVOISIER (1743-1794)
"On the respiration of animals," 1777 122
JOHN SCOTT HALDANE and JOHN GILLIES PRIESTLEY
"Lung ventilation," 1905 126
YANDELL HENDERSON
"Production of shock by loss of carbon dioxide," 1907 . . . 130
JOSEPH BARCROFT
"The respiratory function of the blood," 1925 131
FREDERICK GOWLAND HOPKINS
"On an autoxidisable constituent of the cell," 1921 135

Chapter V: DIGESTION

SANCTORIUS SANCTORIUS (1561-1636)
"Of insensible perspiration," 1614 140
GASPARO ASELLI (1581-1626)
"Discovery of the lacteal veins," 1622 145
REGNER de GRAAF (1641-1673)
"In what manner the pancreatick juice was found out," 1664 . . 146
RENÉ ANTOINE FERCHAULT DE RÉAUMUR (1683-1757)
"On the digestion of birds," 1752 152
LAZARO SPALLANZANI (1729-1799)
"On digestion," 1782 155
WILLIAM CUMBERLAND CRUIKSHANK (1745-1800)
"The anatomy of the absorbing vessels of the human body," 1786 . 159
WILLIAM PROUT (1785-1850)
"On the nature of the acid and saline matters in the stomachs of animals," 1824 163
WILLIAM BEAUMONT (1785-1853)
"On the gastric juice and the physiology of digestion," 1833 . . 164
IVAN PETROVITCH PAVLOV
"The work of the digestive glands," 1910 170
WALTER BRADFORD CANNON
"The movements of the stomach studied by means of the Röntgen rays," 1898 174
WILLIAM MADDOCK BAYLISS (1866-1924) and ERNEST HENRY STARLING (1866-1927)
"The mechanism of pancreatic secretion," 1902 178

Chapter VI: MUSCLE AND PERIPHERAL NERVES

GALEN (131-201 A.D.)
"De motu musculorum" 181
WILLIAM CROONE (1633-1684)
"On the structure of muscle," 1675 185
THOMAS WILLIS (1621-1675)
"On muscular motion," 1670 192
FRANCIS GLISSON (1597-1677)
"De ventriculo et intestinis," 1691 199
GIOVANNI ALFONSO BORELLI (1608-1679)
"De motu animalium," 1680 202
ALEXANDER STUART (1673-1742)
"On muscular motion," 1739 206
ALOYSIO L. GALVANI (1737-1798)
"Concerning electrical forces in muscular movement," 1791 . . 209
HENRY PICKERING BOWDITCH (1840-1911)
"All-or-none response of heart muscle," 1871 213
WALTER MORLEY FLETCHER and FREDERICK GOWLAND HOPKINS
"Lactic acid in muscle," 1907 214
LOUIS LAPICQUE
"Chronaxie," 1908 218
ALEXANDER FORBES and ALAN GREGG
"Action currents of the Flexion Reflex," 1915 220
FREDERICK HAVEN PRATT
"The all-or-none principle in graded response of skeletal muscle," 1917 221
ARCHIBALD VIVIAN HILL and WILLIAM HARTREE
"The four phases of heat-production muscle," 1920 223
GENICHI KATO
"Theory of decrementless conduction," 1924 225
JOSEPH ERLANGER and HERBERT SPENCER GASSER
"Compound nature of nerve action currents," 1924 229
EDGAR DOUGLAS ADRIAN and YNGVE ZOTTERMAN
"On sensory nerves," 1926 232

Chapter VII: THE CENTRAL NERVOUS SYSTEM

RENÉ DESCARTES (1596-1650)
"De homine," 1662 236
ROBERT WHYTT (1714-1766)
"On the vital and other involuntary motions of animals," 1751 . . 242

GEORGIUS PROCHASKA (1749-1820)

"Involuntary motions reflected from the sensorium commune," 1780-1784 247

ALEXANDER WALKER (1779-1852)

"New anatomy and physiology of the brain in particular, and of the nervous system in general," 1809 250

CHARLES BELL (1774-1842)

"Idea of a new anatomy of the brain," 1811 251

FRANÇOIS MAGENDIE (1783-1855)

"On the functions of the roots of the spinal nerves," and "On the functions of the roots of the nerves which arise from the spinal marrow," 1822 258

HERBERT MAYO (1796-1852)

"Anatomical and physiological commentaries," 1823 265

MARIE-JEAN-PIERRE FLOURENS (1794-1867)

"On the properties and functions of the nervous system in vertebrate animals," 1824 266

MARSHALL HALL (1790-1857)

"These motions independent of sensation and volition," 1832 . . 271

JOHANNES MÜLLER (1801-1858)

"Of the peculiar properties of individual nerves," 1838 274

ERNST HEINRICH WEBER (1795-1878) and EDUARD FRIEDRICH WEBER (1806-1871)

"Experiments by which it is proved that when stimulated with a rotatory electromagnetic apparatus the vagus nerves slow down and, to a considerable extent, interrupt the heart-beat," 1845 . . . 276

C. E. BROWN-SÉQUARD (1817-1894)

"On the physiology and pathology of the central nervous system," 1860 278

DAVID FERRIER (1843-1928)

"The functions of the brain," 1876 281

CHARLES SCOTT SHERRINGTON

"Correlation of reflexes and the principle of the common path," 1904; "On the proprioceptive system, especially in its reflex aspect," 1906; in conjunction with E. G. T. LIDDELL, "Reflexes in response to stretch (myotatic reflexes)," 1925 284

HARVEY CUSHING

"Faradic stimulation of the postcentral gyrus," 1909 289

RUDOLPH MAGNUS (1872-1927)

"Animal posture," 1925 292

Chapter VIII: MISCELLANEOUS

CAPTAIN JAMES COOK (1728-1779)
"On the method taken for preserving the health of the crew of H.M.S. *Resolution,*" 1776 296
CARL von VOIT (1831-1908)
"On metabolism," 1902 297
FREDERICK GOWLAND HOPKINS
"Feeding experiments illustrating the importance of accessory factors in normal dietaries," 1907-1912 299
CASIMIR FUNK
"On the chemical nature of the substance which cures polyneuritis in birds induced by a diet of polished rice," 1911 302
GEORGE OLIVER and EDWARD SHARPEY SCHAFER
"On the physiological action of extract of the suprarenal capsules," 1894 304
FREDERICK G. BANTING, CHARLES H. BEST and JOHN J. R. MACLEOD
"The internal secretion of the pancreas," 1922 305

* * * * *

CLAUDE BERNARD (1813-1878)
"Leçons sur les phénomènes de la vie," 1878 307
INDEX 311

ILLUSTRATIONS

Frontispiece. Helmholtz at the age of 27, the year after the publication of his memoir on the conservation of energy. (From L. Koenigsberger's *Hermann von Helmholtz,* Bd. 1, Braunschweig, 1903) . . . . *facing page* iii

Chapter I

Figure 1 The title-page of the tract appended to the second edition of the *Spring and Weight of the Air,* 1662, in which Boyle's law is set forth 7
Figure 2 Boyle's original table proving the reciprocal relation between the volume and pressure of a gas 8
Figure 3 Boyle's first air-pump. (From the first edition of the *Spring and Weight of the Air,* Oxford, 1660) 9
Figure 4 Perrin's chart illustrating Brownian movement of three suspended particles of mastic obtained by joining with straight lines their positions at intervals of 30 seconds . . . 17
Figure 5 The title-page of the first edition of Helmholtz's memoir on the conservation of energy (Berlin, 1847) 19
Figure 6 Ernest Henry Starling (1866-1927) 27

Chapter II

Figure 7 The title-page of Joseph Browne's (*fl.*1700) Lecture against the circulation of the blood, 1701 37
Figure 8 The title-page of the Murr reprint (1790) of the *Christianismi Restitutio* of Servetus, 1553. The reprint is now almost as scarce as the original 43
Figure 9 The pages of Servetus's *Christianismi Restitutio,* 1553, on which occur the description of the pulmonary circulation . 44
Figure 10 The title-page of Fabricius's tract on the valves of the veins, 1603 48
Figure 11A and 11B Harvey's illustration of the valves in the veins, 1628 . . . . 53 and 55
Figure 12 The title-page of Hales's *Statical Essays,* vol. 2, 1733, with one of his tables of blood-pressure 58

Chapter III

Figure 13 Marcello Malpighi (1628-1694) 63
Figure 14 Antony van Leeuwenhoek (1632-1723) from his *Epistolæ ad Societatem Regiam,* Leiden, 1719) 69

Figure 15 Stephen Hales (1677-1761) (from the portrait by Thomas Hudson in the National Portrait Gallery, London) . . 74
Figure 16 The title-page of Whytt's *Physiological Essays,* 1755 . . 80
Figure 17 Albrecht von Haller (1708-1777) 83
Figure 18 The title-page of Haller's *Deux mémoires sur le mouvement du sang,* 1756, in which are recorded his observations on the capillaries 85
Figure 19 The title-page of James Black's *Short inquiry into the capillary circulation of the blood,* 1825 92
Figure 20 Charles Rouget (1824-1904) (from the *Nouvelles Archives du Muséum d'Histoire Naturelle,* Paris, 1904, vol. 6) . . 95

Chapter IV

Figure 21 A. The cancelled title-page of Mayow's *Tractatus Duo* with the date 1669 (original title 1668) 113
B. The separate title of the tract on rickets with date 1668 . 113
C. The first English translation of the tract on rickets . . 113
Figure 22 Mayow's figure, 1668, from his tract on respiration showing the action of the intercostal muscles 115
Figure 23 The title-page of Lower's book on the heart, 1669 . . . 117
Figure 24 The title-page of Priestley's *Experiments and observations upon different kinds of air,* 1774 119
Figure 25 The frontispiece of the first edition of Priestley's *Experiments and observations upon different kinds of air,* 1774, showing some of the receivers in which he collected air. Mice are to be seen in the receiver number 3 121
Figure 26 The first page of Lavoisier's paper announcing the discovery of oxygen *(Hist. Acad. des Sciences,* Paris, 1775, p. 520) . 123
Figure 27 The table from Haldane and Priestley's paper on the influence of CO_2 on the respiratory centre *(Jour. Physiol.,* 1905, vol. 32, p. 249) 127

Chapter V

Figure 28 The Bassanus engraving of Aselli at the age of 42 which is to be found in a few copies of the "De lactibus," 1627 . . 144
Figure 29 De Graaf at 25 (from the first edition of his *De virorum organis generationi,* 1668) 147
Figure 30 De Graaf's engraving of the pancreas and the opening of the pancreatic duct (from the "Succi Pancreatici," 1671) . . 150
Figure 31 De Graaf's illustration of a temporary pancreatic fistula with collecting vessel (from "Succi Pancreatici," 1671) . . 151
Figure 32 Dickinson's engraving of William Cruikshank . . . 158
Figure 33 The title-page of Cruikshank's book on the lymphatics, 1786 159
Figure 34 William Beaumont at the age of 66 (from an old daguerreotype; obtained through the courtesy of Dr. Samuel Harvey) . 166

Figure 35 A photograph of Pavlov taken at the XIIIth International
Figure 36 Cannon's original tracings of the outlines of a cat's stomach
Physiological Congress, just before his 80th birthday . . 171
at successive intervals following a bismuth meal *(Amer. Jour. Physiol.,* vol. 1, 1898, pp. 369-372) 177
Figure 37 Bayliss and Starling's original figure showing the effect on pancreatic secretion and blood-pressure of the intravenous injection of an acid extract of jejunal mucous membrane *(Jour. Physiol.,* vol. 28, 1902, p. 331) 179

Chapter VI

Figure 38 The title-page of one of the numerous 17th century tracts dealing with the physiology of muscle. Boulton's work was a small octavo of 116 pages and it contains an excellent summary of knowledge then existing 181
Figure 39 William Croone (1633-1684). The portrait which hangs in the Censor's room at the Royal College of Physicians, London (obtained through the courtesy of the College) . . . 187
Figure 40 The title-page of the first edition of Croone's anonymous tract on muscular motion 189
Figure 41 Croone's diagram illustrating his beliefs concerning the relation of the circulation and nerve supply of muscle to contraction and the direction of forces exerted by certain muscles at the elbow (from the *De ratione motus musculorum,* 1664) 190
Figure 42 Thomas Willis (1621-1675), the discoverer of the circle of Willis 194
Figure 43 Francis Glisson (1597-1677). The Bodleian portrait which now hangs in the Radcliffe Scientific Library, Oxford (obtained through the courtesy of Bodley's Librarian) . . 198
Figure 44 The title-page of Glisson's book on the stomach and guts, in which is recorded his memorable experiment on the constancy of muscle volume during activity. In this work also Glisson sets forth at length his theory of irritability 200
Figure 45 The title-page of the first volume of Borelli's book on the movements of animals 203
Figure 46 The title-page of the first Croonian Lecture on muscular motion, 1739 206
Figure 47 Stuart's diagram illustrating the motions induced in a decapitated frog on compression of the spinal medulla. He fancied that the movements were due to pressing fluid into the nerves (from the first Croonian Lecture, 1739) . . 207
Figure 48 The title-page of Galvani's book on animal electricity, 1792 210
Figure 49 The figure from Galvani's book which is referred to in the passage quoted 211

Figure 50 Henry Pickering Bowditch (1840-1911) (from W. B. Cannon's memoir in the *Proc. Nat. Acad.*, vol. 17, pp. 183-196, 1924) 215

Chapter VII

Figure 51 The title-page of the first edition of Descartes' *De homine*, 1662, which contains the passages on reflex action, reciprocal innervation and the pineal gland as the seat of the soul . . 237
Figure 52 A. Descartes' original diagrams illustrating reciprocal innervation of the eye muscles. B. One of Descartes' diagrams illustrating the effect of light upon the rational soul lying within the pineal 239
Figure 53 Descartes' excellent figure of the heart with one of the flaps up showing the corda tendinae. This is one of the earliest instances of the use of superimposed drawings to illustrate successive anatomical layers 241
Figure 54 The portrait of Whytt which hangs in the Royal College of Physicians, Edinburgh 244
Figure 55 The title-page of Robert Whytt's book in which the theory of reflex action was set forth, 1751 246
Figure 56 François Magendie (1783-1855) 260
Figure 57 Marshall Hall (1790-1857) (from the engraved frontispiece to the *Memoirs of Marshall Hall* by his widow. London: 1861) 270
Figure 58 The title-page of Omodei's *Annali* which contained the announcement of the Webers of the inhibitory action of the vagus 277
Figure 59 The title-page of Brown-Séquard's paper on the crossing of sensory tracts in the spinal cord (obtained through the courtesy of the Royal Society) 279
Figure 60 The motor and sensory areas as first delineated experimentally by Cushing in a conscious human being *(Brain,* 1909, vol. 125, p. 6) 291

SELECTED READINGS
IN THE HISTORY OF
PHYSIOLOGY

CHAPTER I

GENERAL PRINCIPLES

PHYSIOLOGIA in ancient times signified the study of all natural phenomena, but in the 17th and 18th centuries the term came gradually to be restricted to include only the functions of living organisms. Progress in knowledge of vital activities, however, has been conditioned largely by the growth of physics and chemistry; indeed, physiology has been defined by some as the application of the laws of physics and chemistry to life, and it is strikingly true that in the early days the history of the subject consisted largely of interpretations of vital phenomena in terms of some newly discovered physical or chemical principle. Knowledge of the gas laws for instance was essential to an understanding of the way in which substances pass from the blood to tissue through the capillary walls, and these generalizations are required also for the interpretation of the activity of the kidney. It is therefore fitting that a selection of passages illustrating the history of physiology should include the first description of Boyle's law, Helmholtz's enunciation of the principle of the conservation of energy, van't Hoff and Arrhenius's elucidation of the nature of solutions, and other contributions of this character.

Though in the past physiology has leaned heavily upon its more exact sister sciences, it is undoubtedly true that in the future new discoveries in the realm of physics and chemistry will have a less direct influence than formerly upon the advancement of physiology. In fact it is likely that progress will come through study of the peculiar and limited conditions required for the analysis of vital processes, rather than from application of the newer developments in the more exact sciences. Selection from important generalizations in pure science has therefore been largely restricted to the period before the twentieth century when their influence upon the development of physiological thought was often immediate and very great.

JEAN REY

Jean Rey (circa 1575-1645), a native of Bergerac in the present Department of Dordogne in France, was a physiologist who occupied himself with investigations in what we should now term physical chemistry. It was Rey who first proved that metals increased in weight on "calcination." Two pounds six ounces of the finest English tin, after six hours' calcination, increased seven ounces in weight, while a similar quantity of lead acquired one ounce in the pound less than this. He argued that the gain in weight came from the union of metals with the air, and his inference might well have led him to the modern theory of combustion. His literary style is amusing and the following translation from the *Alembic Club Reprint* (No. 11, 1904) will serve to indicate the nature of his argument and his style of writing.[1]

Essay XVI

FORMAL RESPONSE TO THE QUESTION, WHY TIN AND LEAD INCREASE IN WEIGHT WHEN THEY ARE CALCINED

Now I have made the preparations, nay, laid the foundations for my answer to the question of the sieur Brun, which is, that having placed two pounds six ounces of fine English tin in an iron vessel and heated it strongly on an open furnace for the space of six hours with continual agitation and without adding anything to it, he recovered two pounds thirteen ounces of a white calx; which filled him at first with amazement, and with a desire to know whence the seven ounces of surplus had come. And to increase the difficulty, I say that it is necessary to enquire not only whence these seven ounces have come, but besides them what has replaced the loss of weight which occurred necessarily from the increase of volume of the tin on its conversion into calx, and from the loss of the vapours and exhalations which were given off. To this question, then, I respond and sustain proudly, resting on the foundations already laid, "That this increase in weight comes from the air, which in the vessel has been rendered denser, heavier, and in some measure adhesive, by the vehement and long-continued heat of the furnace: which air mixes with the calx (frequent agitation aiding) and becomes attached to its most minute particles: not otherwise than water makes heavier sand which you throw into it and agitate, by moistening it and adhering to the smallest of its grains." I fancy there are many who would have been alarmed by the sole mention of this response if I had given it at the beginning, who will now willingly receive it, being as it were tamed and rendered tractable by the evident truth of the preceding Essays. For those without doubt whose minds were preoccupied with the opinion that air was light, would have rushed to oppose it. Why (they would have said) does not one extract cold from heat, white from black, light from darkness, since so much heaviness is extracted from air, a thing inherently light? And those who chanced to have bestowed their credence on the heaviness of air, would not have been able to persuade themselves that it can ever increase weight, being balanced in itself. On this account I was constrained to show that air had weight; which was recognisable by other means than the balance: and that even with the latter, a portion previously changed and made denser could manifest its weight. All this I have done as briefly as I found possible, and without advancing anything not strictly germane to this matter: to elucidate which at all points it only remains for me to state and refute succinctly some opinions which others have held or might hold; and to resolve the objections which might be made to my answer.

---

[1] Rey, J. *Essays de Jean Rey, docteur en medecine, sur la recherche de la cause pour laquelle l'estain et le plomb augmentent de poids quand on les calcine.* Bazas, 1630; reprinted in Paris, 1777.

[The author then considers possible objections under the following headings]

Essay XVII. That it is not the disappearance of the celestial heat giving life to the lead, or the death of the latter, which augments its weight on calcination.

Essay XVIII. That it is not the consumption of the aërated particles which augments the weight of the lead.

Essay XIX. That it is not soot which augments the weight of the calx.

Essay XX. That the augmentation of the calx of tin and lead does not come from the vessel.

Essay XXI. That it is not the vapours from the charcoal that augment the weight.

Essay XXII. That it is not the volatile salt of the charcoal which augments the weight.

Essay XXIII. That the mercurial volatile salt is not the cause of this augmentation.

Essay XXIV. That it is not humidity attracted by the calx which augments its weight.

Essay XXV. By a single experiment all opinions contrary to mine are entirely destroyed.

Essay XXVI. Why the calx does not increase in weight infinitely.

Essay XXVII. Why all other calces and ashes do not increase in weight.

Essay XXVIII. Whether lead increases in weight as well as tin.

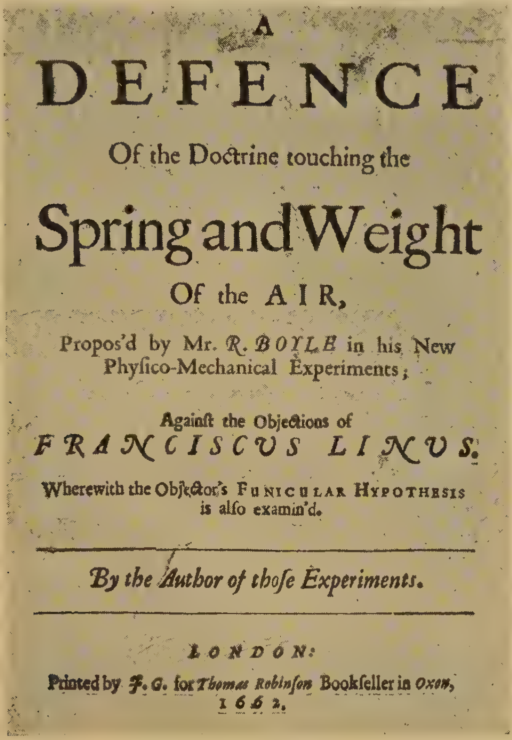
CONCLUSION

Behold now this truth, whose brilliance strikes the eye, which I have drawn from the deepest dungeons of obscurity. This it is to which the path has been hitherto inaccessible. This it is which has distressed with toil so many learned men, who, wishing to know it, have striven to clear the difficulties which held it encircled. Cardan, Scaliger, Fachsius, Cæsalpinus, Libavius, have curiously sought it, but never perceived it. Others may be on its quest, but vainly if they fail to follow the road which I first of all have made clear and royal: all others being but thorny footpaths and inextricable byways which lead never to the goal. The labour has been mine; may the profit be to the reader, and to God alone the glory.

ROBERT BOYLE

THE HONOURABLE ROBERT BOYLE (1627-1692), who by a nineteenth century wit was described as the "seventh son of the Earl of Cork and father of modern chemistry," made in the course of a brief life more fundamental discoveries in the broad field of science than any individual is likely ever to make again. In 1660 he weighed the air, proved that it would support a column of 29 inches of mercury, and described the first barometer; in 1661 appeared his memorable book *The Sceptical Chymist* which marks the beginning of modern chemistry; in 1662, in the passage which we give below, he established the reciprocal relation between the pressure of a gas and the volume which it occupies; in 1664 fundamental studies upon colours and deflection of light through prisms appeared, and in the following year he invented a spirit thermometer. In addition to these activities he was carrying on important investigations upon the physiology of respiration referred to in another chapter. It may also be mentioned that in 1675 he wrote the first treatise in English on "electricity."

The description of Boyle's law did not appear in the first edition of *The Spring and Weight of the Air* (1660) as it is sometimes stated. It was brought forward in a separate tract, appended to the second edition of this work (1662), entitled *A Defence of the Doctrine touching the Spring and Weight of the Air, Propos'd by Mr. R. Boyle in his New Physico-Mechanical Experiments; Against the Objections of Franciscus Linus. Wherewith the Objector's Funicular Hypothesis is also examin'd* (Fig. 1). In a tract published in 1661, Linus had objected to Boyle's inferences concerning the weight of the air and the enunciation of the reciprocal relation between the pressure of a gas and the volume which it occupies was used by Boyle as an argument in answer to his critic. The passage in the "Defence" occurs in Chapter V, which is entitled "Two new Experiments touching the measure of the Force of the Spring of Air compress'd and dilated," and is to be found on pages 58-60 of the first edition. A photograph of Boyle's original table is given in Fig. 2, and the plate of his air-pump in Fig. 3.



A
DEFENCE
Of the Doctrine touching the
Spring and Weight
Of the AIR,
Propos'd by Mr. *R. BOYLE* in his New
Phyſico-Mechanical Experiments;
Againſt the Objections of
FRANCISCUS LINUS.
Wherewith the Objector's FUNICULAR HYPOTHESIS
is alſo examin'd.

By the Author of thoſe Experiments.

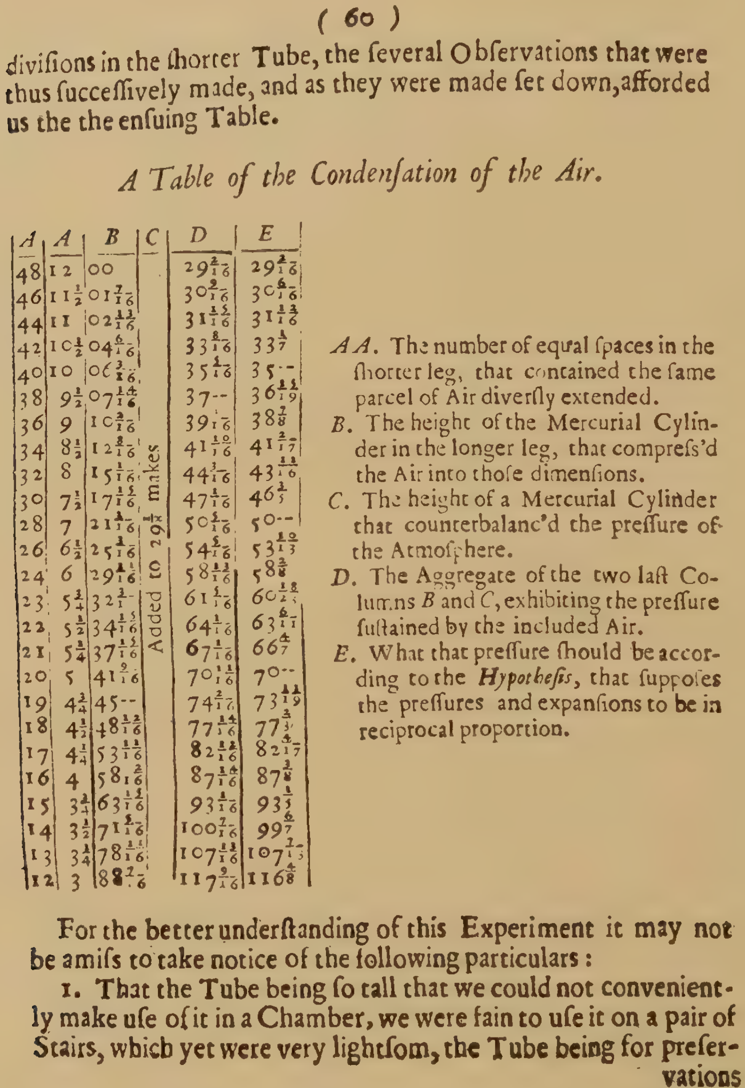
LONDON:
Printed by *J. G.* for *Thomas Robinſon* Bookſeller in *Oxon*,
1662.

FIGURE 1. The title-page of the tract appended to the second edition of the *Spring and Weight of the Air,* 1662, in which Boyle's law is set forth.

CHAPTER V

TWO NEW EXPERIMENTS TOUCHING THE MEASURE OF THE FORCE OF THE SPRING OF AIR COMPRESS'D AND DILATED

The other thing that I would have considered touching our Adversaries *Hypothesis* is, That it is *needless.* For whereas he denies not that the Air has some Weight and Spring, but affirms that it is very insufficient to perform such great matters as the counterpoising of a Mercurial Cylinder of 29. Inches, as we teach that it may: We shall now endeavour to



(60)

diviſions in the ſhorter Tube, the ſeveral Obſervations that were thus ſucceſſively made, and as they were made ſet down, afforded us the the enſuing Table.

A Table of the Condenſation of the Air.

A	*A*	*B*	*C*	*D*	*E*
48	12	00	Added to $29\frac{1}{8}$ makes	$29\frac{2}{16}$	$29\frac{2}{16}$
46	$11\frac{1}{2}$	$01\frac{7}{16}$		$30\frac{9}{16}$	$30\frac{6}{16}$
44	11	$02\frac{13}{16}$		$31\frac{15}{16}$	$31\frac{12}{16}$
42	$10\frac{1}{2}$	$04\frac{6}{16}$		$33\frac{8}{16}$	$33\frac{1}{7}$
40	10	$06\frac{3}{16}$		$35\frac{5}{16}$	35--
38	$9\frac{1}{2}$	$07\frac{14}{16}$		37--	$36\frac{12}{19}$
36	9	$10\frac{2}{16}$		39 [illegible]	$38\frac{7}{8}$
34	$8\frac{1}{2}$	$12\frac{8}{16}$		$41\frac{10}{16}$	$41\frac{2}{17}$
32	8	$15\frac{1}{16}$		$44\frac{3}{16}$	$43\frac{11}{16}$
30	$7\frac{1}{2}$	$17\frac{15}{16}$		$47\frac{1}{16}$	$46\frac{3}{5}$
28	7	$21\frac{3}{16}$		$50\frac{5}{16}$	50--
26	$6\frac{1}{2}$	$25\frac{3}{16}$		$54\frac{5}{16}$	$53\frac{10}{13}$
24	6	$29\frac{11}{16}$		$58\frac{13}{16}$	$58\frac{2}{8}$
23	$5\frac{3}{4}$	$32\frac{3}{16}$		$61\frac{5}{16}$	$60\frac{18}{23}$
22	$5\frac{1}{2}$	$34\frac{15}{16}$		$64\frac{1}{16}$	$63\frac{6}{11}$
21	$5\frac{1}{4}$	$37\frac{15}{16}$		$67\frac{1}{16}$	$66\frac{4}{7}$
20	5	$41\frac{9}{16}$		$70\frac{11}{16}$	70--
19	$4\frac{3}{4}$	45--		$74\frac{2}{16}$	$73\frac{11}{19}$
18	$4\frac{1}{2}$	$48\frac{12}{16}$		$77\frac{14}{16}$	$77\frac{2}{3}$
17	$4\frac{1}{4}$	$53\frac{11}{16}$		$82\frac{12}{16}$	$82\frac{4}{17}$
16	4	$58\frac{2}{16}$		$87\frac{14}{16}$	$87\frac{3}{8}$
15	$3\frac{3}{4}$	$63\frac{15}{16}$		$93\frac{1}{16}$	$93\frac{1}{5}$
14	$3\frac{1}{2}$	$71\frac{5}{16}$		$100\frac{7}{16}$	$99\frac{6}{7}$
13	$3\frac{1}{4}$	$78\frac{11}{16}$		$107\frac{13}{16}$	$107\frac{7}{13}$
12	3	$88\frac{7}{16}$		$117\frac{9}{16}$	$116\frac{4}{8}$

AA. The number of equal ſpaces in the ſhorter leg, that contained the ſame parcel of Air diverſly extended.

B. The height of the Mercurial Cylinder in the longer leg, that compreſs'd the Air into thoſe dimenſions.

C. The height of a Mercurial Cylinder that counterbalanc'd the preſſure of the Atmoſphere.

D. The Aggregate of the two laſt Columns *B* and *C*, exhibiting the preſſure ſuſtained by the included Air.

E. What that preſſure ſhould be according to the *Hypotheſis*, that ſuppoſes the preſſures and expanſions to be in reciprocal proportion.

For the better underſtanding of this Experiment it may not be amiſs to take notice of the following particulars:

1. That the Tube being ſo tall that we could not conveniently make uſe of it in a Chamber, we were fain to uſe it on a pair of Stairs, which yet were very lightſom, the Tube being for preſer-

vations

FIGURE 2. Boyle's original table proving the reciprocal relation between the volume and pressure of a gas.

manifest by Experiments purposely made, that the Spring of the Air is capable of doing far more than 'tis necessary for us to ascribe to it, to salve the *Phænomena* of the *Torricellian* Experiment.

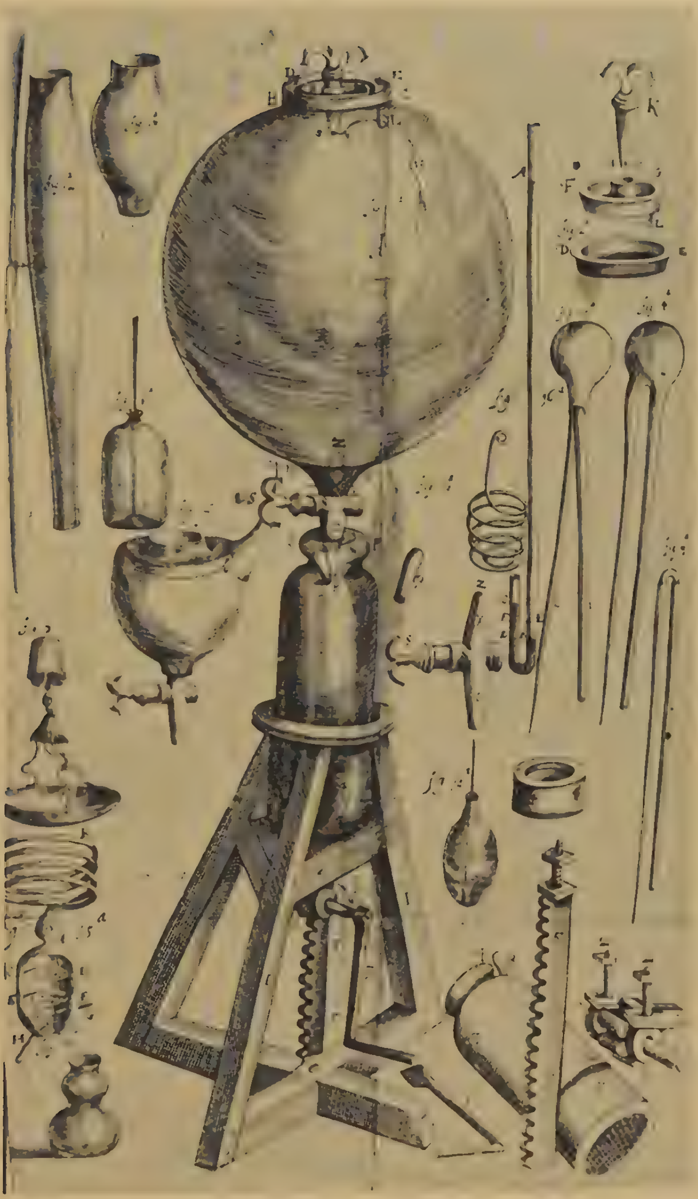


FIGURE 3. Boyle's first air-pump. (From the first edition of the *Spring and Weight of the Air,* Oxford, 1660).

We took then a long Glass-Tube, which by a dexterous hand and the help of Lamp was in such a manner crooked at the bottom, that the part turned up was almost parallel to the rest of the Tube, and the Orifice of this shorter leg of the Siphon (if I may so call the whole Instrument) being Hermetically seal'd, the length of it was divided into Inches, (each of which was subdivided into eight parts) by a straight list of paper, which containing those Divisions was carefully pasted all along it: then putting in as much Quicksilver as served to fill the Arch or bended part of the Siphon, that the *Mercury* standing in a level might reach in the one leg to the bottom of the divided paper, and just to the same height or horizontal line in the other; we took care, by frequently inclining the Tube, so that the Air might freely pass from one leg into the other by the sides of the Mercury, (We took (I say) care) that the Air at last included in the shorter Cylinder should be of the same laxity with the rest of the Air about it. This done, we began to pour Quicksilver into the longer leg of the Siphon, which by its weight pressing up that in the shorter leg, did by degrees streighten the included Air: and continuing this pouring in of Quicksilver till the Air in the shorter leg was by condensation reduced to take up but half the space it possess'd (I say, *possess'd,* not *fill'd*) before; *we cast our eyes upon the longer leg of the Glass, on which was likewise pasted a list of Paper carefully divided into Inches and parts, and we observed, not without delight and satisfaction, that the Quicksilver in that longer part of the Tube was 29. Inches higher then the other.*[2] Now that this Observation does both very well agree with and confirm our *Hypothesis,* will be easily discerned by him that takes notice that we teach, and Monsieur *Paschall* and our *English* friends Experiments prove, that the greater the weight is that leans upon the Air, the more forcible is its endeavour of Dilatation, and consequently its power of resistance, (as other Springs are stronger when bent by greater weights.) For this being considered it will appear to agree rarely-well with the *Hypothesis,* that as according to it the Air in that degree of density and correspondent measure of resistance to which the weight of the incumbent Atmosphere had brought it, was able to counter-balance and resist the pressure of a Mercurial Cylinder of about 29. Inches, as we are taught by the *Torricellian* Experiment; so here the same Air being brought to a degree of density about twice as great as that it had before, obtains a Spring twice as strong as formerly. As may appear by its being able to sustain or resist a Cylinder of 29. Inches in the longer Tube, together with the weight of the Atmospherical Cylinder, that lean'd upon those 29. Inches of *Mercury;* and, as we just now inferr'd from the *Torricellian* Experiment, was equivalent to them.

---

[2] Italics in these four lines by the editor.

We were hindered from prosecuting the tryal at that time by the casual breaking of the Tube. But because an accurate Experiment of this nature would be of great importance to the Doctrine of the Spring of the Air, and has not yet been made (that I know) by any man; and because also it is more uneasie to be made then one would think, in regard of the difficulty as well of procuring crooked Tubes fit for the purpose, as of making a just estimate of the true place of the Protuberant *Mercury's* surface; I suppose it will not be unwelcome to the Reader, to be informed that after some other tryals, one of which we made in a Tube whose longer leg was perpendicular, and the other, that contained the Air, parallel to the Horizon, we at last procured a Tube of the Figure exprest in the Scheme; which Tube, though of a pretty bigness, was so long, that the Cylinder whereof the shorter leg of it consisted admitted a list of Paper, which had before been divided into 12. Inches and their quarters, and the longer leg admitted another list of Paper of divers foot in length, and divided after the same manner: then Quicksilver being poured in to fill up the bended part of the Glass, that the surface of it in either leg might rest in the same Horizontal line, as we lately taught, there was more and more Quicksilver poured into the longer Tube; and notice being watchfully taken how far the *Mercury* was risen in that longer Tube, when it appeared to have ascended to any of the divisions in the shorter Tube, the several Observations that were thus successively made, and as they were made set down, afforded us the ensuing Table.

CHARLES BLAGDEN

Sir Charles Blagden (1748-1820). The spectacular and well conceived experiments[3] of Blagden upon the ability of the body to withstand dry heat are seldom referred to in modern literature upon heat regulation. His account, published at the age of 26, was noteworthy because it contains the first statement

[3] Blagden, C. "Experiments and observations in an heated room." *Philosophical Transactions of the Royal Society,* vol. 65, pp. 111-124; 484-494, 1775. A reprint of these two papers formerly belonging to Sir Joseph Banks has recently come into the editor's possession. They are bound together and paged continuously from 1-24. Banks's autograph, "J:J: Banks 1775." and his library stamp appear on the first page.

of the importance of perspiration for maintaining the constancy of body temperature. The cooling effect of evaporation was proved by covering a vessel of water with a layer of oil which caused it to boil when placed in a warm atmosphere; otherwise the temperature of the water did not rise above 140° even though the atmosphere was raised to 260° (Fahrenheit). The incidental observation of the effect of salt in raising the boiling point of water undoubtedly led Blagden several years later (1788) to the memorable discovery that the depression of the freezing point of water by inorganic salts is proportional to the amount dissolved. Sir Joseph Banks who acted as a subject for Blagden's observations was for 41 years President of the Royal Society of London, and Blagden himself acted for a long period as its secretary.

EXPERIMENTS AND OBSERVATIONS IN AN HEATED ROOM

By Charles Blagden, M.D. F.R.S.

Paper I

Read at the ROYAL SOCIETY, February 16, 1774

About the middle of January, several gentlemen and myself received an invitation from Dr. George Fordyce, to observe the effects of air heated to a much higher degree than it was formerly thought any living creature could bear. We all rejoiced at the opportunity of being convinced, by our own experience, of the wonderful power with which the animal body is endued, of resisting an heat vastly greater than its own temperature; and our curiosity was not a little excited to observe the circumstances attending this remarkable power. . . . .

January 23. The honourable Captain Phipps, Mr. Banks, Dr. Solander, and myself, attended Dr. Fordyce to the heated chamber, which had served for many of his experiments with dry air. We went in without taking off any of our cloaths. It was an oblong-square room, fourteen feet by twelve in length and width, and eleven in height, heated by a round stove, or *cockle,* of cast iron, which stood in the middle, with a tube for the smoke carried from it through one of the side walls. When we first entered the room, about 2 o'clock in the afternoon, the quicksilver in a thermometer which had been suspended there stood above the 150th degree. . . . . Soon afterwards Dr. Solander entered the room alone, and saw the thermometer at 210°; but, during three minutes that he staid there, it sunk 196°. Mr. Banks closed the whole, by going in when the thermometer stood above 211°; he remained there seven minutes, in which time the quicksilver had sunk to 198°; but cold air had been let into the room, by a person who went in and came out again during Mr. Banks's stay.

The air heated to these high degrees felt unpleasantly hot, but could be born very well. Our most uneasy feeling was a sense of scorching on the face and legs; our legs particularly suffered extremely, by being exposed more fully than any other part to the body of the stove, heated red-hot by the fire within. Our respiration was not at all affected; it became neither quick nor laborious; the only difference was a want of that refreshing sensation which accompanies a full inspiration of cool air. Our time was so taken up with other observations that we did not count our pulses by the watch: mine, to the best of my judgment by feeling it, beat at the rate of 100 pulsations in a minute, near the end of the first experiment: and Dr. Solander's made 92 pulsations in a minute soon after we had gone out of the heated room. Mr. Banks sweated profusely, but no one else; my shirt was only damp at the end of the experiment.

But the most striking effects proceeded from our power of preserving our natural temperature. Being now in a situation in which our bodies bore a very different relation to the surrounding atmosphere from that to which we had been accustomed, every moment presented a new phænomenon. Whenever we breathed on a thermometer the quicksilver sunk several degrees. Every expiration, particularly if made with any degree of violence, gave a very pleasant impression of coolness to our nostrils scorched just before by the hot air rushing against them when we inspired. In the same manner our now cold breath agreeably cooled our fingers whenever it reached them. Upon touching my side, it felt cold like a corpse; and yet the actual heat of my body, tried under my tongue and by applying closely the thermometer to my skin, was 98°, about a degree higher than its ordinary temperature. . . .

[At 260°] The air felt very hot, but still by no means to such a degree as to give pain: on the contrary, I had no doubt of being able to support a much greater heat; and all the gentlemen present, who went into the room, were of the same opinion. I sweated, but not very profusely. For seven minutes my breathing continued perfectly good; but after that time I began to feel an oppression in my lungs, attended with a sense of anxiety; which gradually increasing for the space of a minute, I thought it most prudent to put an end to the experiment, and immediately left the room. My pulse, counted as soon as I came into the cool air, for the uneasy feeling rendered me incapable of examining it in the room, was found to beat at the rate of 144 pulsations in a minute, which is more than double its ordinary quickness. . . . .

To prove that there was no fallacy in the degree of heat shewn by the thermometer, but that the air which we breathed was capable of producing all the well-known effects of such an heat on inanimate matter, we put some eggs and a beef-steak upon a tin frame, placed near the standard thermometer, and farther distant from the cockle than from the wall of the room. In about twenty minutes the eggs were taken out, roasted quite hard; and in forty-seven minutes the steak was not only dressed, but almost dry. Another beaf-steak was rather over-done in thirty-three minutes. In the evening, when the heat was still greater, we laid a third beef-steak in the same place: and as it had now been observed, that the effect of the heated air was much increased by putting it in motion, we blew upon the steak with a pair of bellows, which produced a visible change on its surface, and seemed to hasten the dressing; the greatest part of it was found pretty well done in thirteen minutes.

About the middle of the day two similar earthen vessels; one containing pure water, and the other an equal quantity of the same water with a bit of wax, were put upon a piece of wood in the heated room. In one hour and an half the pure water was heated to 140° of the thermometer, whilst that with the wax had acquired an heat of 152°, part of the wax having melted and formed a film on the surface of the water, which prevented the evaporation. The pure water never came near the boiling point, but continued stationary above an hour at a much lower degree; a small quantity of oil was then dropped into it, as had before been done to that with the wax; in consequence of which, the water in both the vessels came at length to boil very briskly. A saturated solution of salt in water put into the room, was found to heat more quickly, and to an higher degree, than pure water, probably because it evaporated less; but it could not be brought to boil till oil was added, by means of which it came toward evening into brisk ebullition, and consequently had acquired an heat of 230°. . . . . Perhaps no experiments hitherto made furnish more remarkable instances of the cooling effect of evaporation than these last facts; a power which appears to be much greater than hath commonly been suspected. The evaporation itself, however, was more considerable in our experiments than it can be in almost any other situation, because the air applied to the evaporating surface was uncommonly hot, and at the same time not more charged with moisture than in its ordinary state.

ROBERT BROWN

ROBERT BROWN (1773-1858), the distinguished English botanist who discovered the nucleus of plant cells (1831) and the significance of pollen in fecundation, was the private librarian of Sir Joseph Banks [v. *supra* Sir Charles Blagden]. That he was also the Brown of "Brownian Movement" (agitation of small suspended particles) is not recognized in the official account of his life in the *Dictionary of National Biography.* His original description of the phenomenon,[4] which is given below, was set forth quite casually in the midst of a paper on the pollen of plants. The active "molecules" which he mentions in the title refer to particles of pollen visible with his microscope.

ON THE PARTICLES CONTAINED IN THE POLLEN OF PLANTS

The observations, of which it is my object to give a summary in the following pages, have all been made with a simple microscope, and indeed with one and the same lens, the focal length of which is about $1/32$nd of an inch.

My inquiry on this point was commenced in June 1827, and the first plant examined proved in some respects remarkably well adapted to the object in view.

This plant was Clarckia pulchella, of which the grains of pollen, taken from antheræ full grown, but before bursting, were filled with particles or granules of unusually large size, varying from nearly $1/4000$th to about $1/5000$th of an inch in length, and of a figure between cylindrical and oblong, perhaps slightly flattened, and having rounded and equal extremities. While examining the form of these particles immersed in water, I observed many of them very evidently in motion; their motion consisting not only of a change of place in the fluid, manifested by alterations in their relative positions, but also not unfrequently of a change of form in the particle itself; a contraction or curvature taking place repeatedly about the middle of one side, accompanied by a corresponding swelling or convexity on the opposite side of the particle. In a few instances the particle was seen to turn on its longer axis. These motions were such as to satisfy me, after frequently repeated observation, that they arose neither from currents in the fluid, nor from its gradual evaporation, but belonged to the particle itself.

---

[4] Brown, R. "A brief account of the microscopical observations made in the months of June, July, and August, 1827, on the particles contained in the pollen of plants; and on the general existence of active molecules in organic and inorganic bodies." *Edin. New Philos. Jour.,* vol. 5, pp. 358-371; *Phil. Mag.,* vol. 4, pp. 160-182, 1828 (pp. 161-163).

Grains of pollen of the same plant taken from antheræ immediately after bursting, contained similar subcylindrical particles, in reduced numbers however, and mixed with other particles, at least as numerous, of much smaller size, apparently spherical, and in rapid oscillatory motion.

These smaller particles, or Molecules as I shall term them, when first seen, I considered to be some of the cylindrical particles swimming vertically in the fluid. But frequent and careful examination lessened my confidence in this supposition; and on continuing to observe them until the water had entirely evaporated, both the cylindrical particles and the spherical molecules were found on the stage of the microscope.

* * *

The nature of 'Brownian movement' occupied the minds of many of the best physicists of the nineteenth century, but a satisfactory explanation was not given until 1909, when Jean Perrin, the Professor of Physical Chemistry at the Faculté des Sciences of the University of Paris, published his important paper on "Brownian movement and molecular reality." He pointed out that agitation of suspended particles was an inevitable consequence of their bombardment by molecules dissolved in a given solution, and that Brownian movement afforded in fact most significant evidence in favor of the atomic theory and of the gas laws. The description of one of his observations, and his conclusions are given below.

BROWNIAN MOVEMENT AND MOLECULAR REALITY[5]

By M. JEAN PERRIN

The figure here reproduced (fig. 4) shows three drawings obtained by tracing the segments which join the consecutive positions of the same granules of mastic at intervals of 30 seconds. It is the half of the mean square of such segments which verifies the formula of Einstein. One of these drawings shows 50 consecutive positions of the same granule. They only give a very feeble idea of the prodigiously entangled character of the real trajectory. If the positions were indicated from second to second, each of these rectilinear segments would be replaced by a polygonal contour of 30 sides, relatively as complicated as the drawing here reproduced, and so on. One realises from such examples how near the mathematicians are to the truth in refusing, by logical instinct, to admit the pretended geometrical demonstrations, which are regarded as experimental evidence for the existence of a tangent at each point of a curve . . . . 44. Conclusion.—I think I have given in this Memoir the present state of our knowledge of the Brownian movement and of molecular magnitudes. The personal contributions which I have attempted to bring to this knowledge, both by theory and experiment, will

---

[5] Perrin, J. "Mouvement Brownien et réalité moléculaire." *Annales de Chimie et de Physique,* 8^{me} sér., tom. 18, pp. 1-114, 1909. Translated by F. Soddy, M.A., F.R.S., London; Taylor and Francis, 1910).

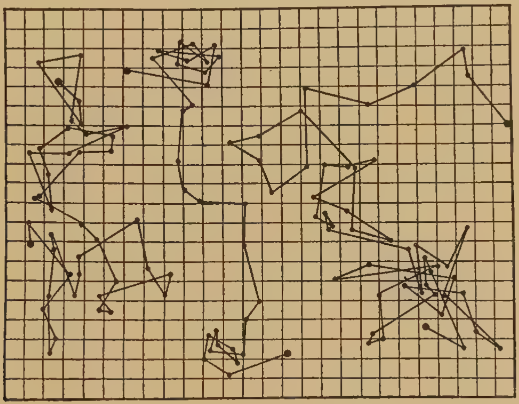


FIGURE 4. Perrin's chart illustrating Brownian movement of three suspended particles of mastic obtained by joining with straight lines their positions at intervals of 30 seconds.

I hope elucidate it, and will show that the observation of emulsions gives a solid experimental basis to molecular theory. The principle results established in the course of this work are in summary:—

The preparation of emulsions with equal spherical granules, of an exactly measured radius, chosen at will;

The extension of Stokes's law to the domain of microscopic magnitudes;

The demonstration that the laws of perfect gases apply to uniform emulsions;

The exact determination, from this experimental fact, of the various molecular magnitudes, and of the charge of the electron;

The experimental confirmation, for the rotations as well as for the translations, of the equipartition of energy, and of the beautiful theoretical investigations of Einstein;

Lastly, arising out of this confirmation, a second exact determination, agreeing with the first of the various molecular magnitudes.

HERMANN VON HELMHOLTZ

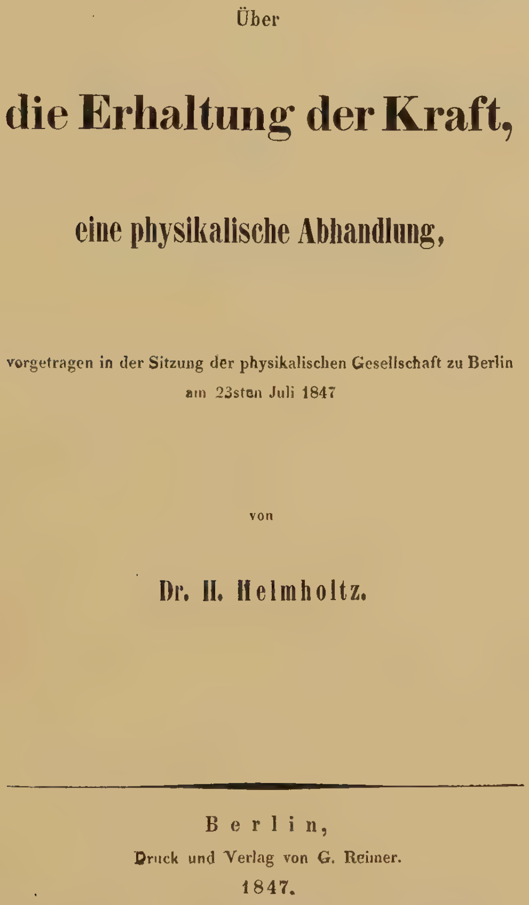
Hermann von Helmholtz (1821-1894), one of the greatest thinkers of all time, had German, French, and English forbears, his mother being descended from William Penn. At the age of 21 Helmholtz became a pupil of Johannes Müller and soon after wrote a neuroanatomical thesis of unusual merit (nerve cells of leeches); at 24 he measured for the first time the heat production of frog muscle; and at 26 he enunciated, independently of his countryman, Robert Mayer, the principle of the conservation of energy. Starting life as a military physician, Helmholtz became, at the age of 28, a professor of physiology at Königsberg and it is often forgotten that he continued to occupy physiological chairs throughout the greater part of his active life (1871). "Medicine," he said in later years, "was once the intellectual home in which I grew up; and even the emigrant best understands and is best understood by his native land" (Garrison). His phenomenal powers of sustained abstract thinking had not been approached in any field of thought since the days of Newton, except possibly by his contemporary Willard Gibbs, who was considerably less versatile. The Helmholtz-Gibbs equation, which they worked out independently, states that the capacity for work of a galvanic cell is equal to the free energy of its electro-chemical equivalent of decomposition. However, one cannot enumerate all of Helmholtz's contributions to physiology; everything he touched, except psychology, was, as if by magic, turned to gold. His paper on the conservation of energy, written early in 1847, was offered to Poggendorff's *Annalen,* but the editor thought ill of so dangerous a speculation and failed to appreciate its true significance. Du Bois Reymond had grasped the importance of the paper and advised Helmholtz to issue it as a separate treatise. G. A. Reimer, the Berlin publisher, was accordingly approached and on du Bois Reymond's recommendation it was immediately accepted, and Helmholtz, to his astonishment, received an honorarium. The following passage[6], taken from the philosophical introduction of this celebrated essay, indicates the extraordinary heights to which Helmholtz had soared at the early age of 26 years.

The Conservation of Energy

The principal contents of the present memoir show it to be addressed to physicists chiefly, and I have therefore thought it judicious to lay down its fundamental principles purely in the form of a physical premise, and, independent of metaphysical considerations, to develop the consequences of these principles, and to submit them to a comparison with what experience has established in the various branches of physics. The deduction of the propositions contained in the memoir may be based on either of two maxims; either on the maxim that it is not possible by any combination whatever of natural bodies to derive an unlimited amount of mechanical force, or on the assumption that all actions in nature can be ultimately referred to attractive or repulsive forces, the intensity of which depends solely on the distances between the points at which the forces are exerted. That both these propositions are identical is shown at the commencement of the memoir itself. Meanwhile the important bearing which they have upon the final aim of the physical sciences may with propriety be made the subject of a special introduction.

---

[6] Helmholtz, H. *Über die Erhaltung der Kraft.* Berlin: G. Reimer, 2 1.,+72 pp. 1847. The translation is that of J. Tyndall given by Francis A. Welby in his English edition of Koenigsberger's *Hermann von Helmholtz,* Oxford: Clarendon Press, xvii+440 pp., 1906 (pp. 39-42). The attention of the reader is directed to the recently published letters of Anna von Helmholtz, which throws much new light upon her husband's career. *Anna von Helmholtz. Ein Lebensbild in briefen.* Herausgegeben von Ellen von Siemens-Helmholtz. Berlin: Verlag für Kulturpolitik, 2 Bd., 344 pp., 266 pp., 1929.



Über

die Erhaltung der Kraft,

eine physikalische Abhandlung,

vorgetragen in der Sitzung der physikalischen Gesellschaft zu Berlin
am 23sten Juli 1847

von

Dr. H. Helmholtz.

Berlin,
Druck und Verlag von G. Reimer.
1847.

FIGURE 5. The title-page of the first edition of Helmholtz's memoir on the conservation of energy (Berlin, 1847).

The problem of the sciences just alluded to is, in the first place, to seek the laws by which the particular processes of nature may be referred to, and deduced from, general rules. These rules—for example, the law of reflection and refraction of light, the law of Mariotte and Gay-Lussac regarding the volumes of gases—are evidently nothing more than general ideas by which the various phenomena which belong to them are connected together. The finding out of these is the office of the experimental portion of our science. The theoretic portion seeks, on the contrary, to evolve the unknown causes of the processes from the visible actions which they present; it seeks to comprehend these processes according to the laws of causality. We are justified, and indeed impelled in this proceeding, by the conviction that every change in nature *must* have a sufficient cause. The proximate causes to which we refer phenomena may, in themselves, be either variable or invariable; in the former case the above conviction impels us to seek for causes to account for the change, and thus we proceed until we at length arrive at final causes which are unchangeable, and which therefore must, in all cases where the exterior conditions are the same, produce the same invariable effects. The final aim of the theoretic natural sciences is therefore to discover the ultimate and unchangeable causes of natural phenomena. Whether all the processes of nature be actually referable to such, or whether nature is capable of being completely comprehended, or whether changes occur which are not subject to the laws of necessary causation, but spring from spontaneity or freedom, this is not the place to decide; it is at all events clear that the science whose object it is to comprehend nature must proceed from the assumption that it is comprehensible, and in accordance with this assumption investigate and conclude until, perhaps, she is at length admonished by irrefragable facts that there are limits beyond which she cannot proceed.

Science regards the phenomena of the exterior world according to two processes of abstraction; in the first place it looks upon them as simple existences, without regard to their action upon our organs of sense or upon each other; in this aspect they are termed *matter.* The existence of matter in itself is to us something tranquil and devoid of action: in it we distinguish merely the relations of space and of quantity (mass), which is assumed to be eternally unchangeable. To matter, thus regarded, we must not ascribe qualitative differences, for when we speak of different kinds of matter we refer to differences of action, that is, to differences in the forces of matter. Matter in itself can therefore partake of one change only, a change which has reference to space, that is, motion. Natural objects are not, however, thus passive; in fact we come to a knowledge of their existence solely from their actions upon our organs of sense, and infer from these actions a something which acts. When, therefore, we wish to make actual application of our idea of matter, we can only do it by means of a second abstraction, and ascribe to it properties which in the first case were excluded from our idea, namely, the capability of producing effects, or, in other words, of exerting *force.* It is evident that in the application of the ideas of matter and force to nature the two former should never be separated: a mass of pure matter would as far as we and nature are concerned be a nullity, inasmuch as no action could be wrought by it either upon our organs of sense or upon the remaining portion of nature. A pure force would be something which must have a basis, and yet which has no basis, for the basis we name matter. It would be just as erroneous to define matter as something which has an actual existence, and force as an idea which has no corresponding reality. Both, on the contrary, are abstractions from the actual, formed in precisely similar ways. Matter is only discernible by its forces, and not by itself.

We have seen above that the problem before us is not to refer back the phenomena of nature to unchangeable final causes. This requirement may now be expressed by saying that for final causes unchangeable forces must be found. Bodies with unchangeable forces have been named in science (chemistry) elements. Let us suppose the universe decomposed into elements possessing unchangeable qualities, the only alteration possible to such a system is an alteration of position, that is, motion; hence the forces can only be moving forces dependent in their action upon conditions of space.

To speak more particularly: the phenomena of nature are to be referred back to motions of material particles possessing unchangeable moving forces, which are dependent upon conditions of space alone. Motion is the alteration of the conditions of space. Motion, as a matter of experience, can only appear as a change in the relative position of at least two material bodies. Force, which originates motion, can only be conceived of as referring to the relation of at least two material bodies toward each other; it is therefore to be defined as the endeavour of two masses to alter their relative position. But the force which two masses exert upon each other must be resolved into those exerted by all their particles upon each other; hence in mechanics we go back to forces exerted by material points. The relation of one point to another, as regards space, has reference solely to their distance apart: a moving force, therefore, exerted by each upon the other, can only act so as to cause an alteration of their distance, that is, it must be either attractive or repulsive.

Finally, therefore, we discover the problem of physical natural science to be, to refer natural phenomena back to unchangeable attractive and repulsive forces, whose intensity depends solely upon distance. The solvability of this problem is the condition of the complete comprehensibility of nature. In mechanical calculations this limitation of the idea of moving force has not yet been assumed: a great number, however, of general principles referring to the motion of compound systems of bodies are only valid for the case that these bodies operate upon each other by unchangeable attractive or repulsive forces; for example, the principle of virtual velocities; the conservation of the motion of the centre of gravity; the conservation of the principle plane of rotation; of the moment of rotation of free systems; and the conservation of *vis viva.* In terrestrial matters application is made chiefly of the first and last of these principles, inasmuch as the others refer to systems which are supposed to be completely free; we shall, however, show that the first is only a special case of the last, which therefore must be regarded as the most general and important consequence of the deduction which we have made.

Theoretical natural science therefore, if she does not rest contented with half-views of things, must bring her notions into harmony with the expressed requirements as to the nature of simple forces, and with the consequences which flow from them. Her vocation will be ended as soon as the reduction of natural phenomena to simple forces is complete, and the proof given that this is the only reduction of which the phenomena are capable.

JAKOBUS HENRICUS VAN'T HOFF

Jakobus Henricus van't Hoff (1852-1911), a distinguished Dutch chemist, arrived at the conclusion in 1885 that the laws of gases were applicable to solutions, and issued in that year a preliminary note in *Kong. Svenska Vetenskaps, Akademisk Handlingar* (vol. 21, Oct. 14, 1885, 41 pp.) entitled "Lois de l'équilibre chimique dans l'état dilué, gazeux ou dissous."

SVANTE ARRHENIUS

Svante Arrhenius (1859-1927) in 1883, at the age of twenty-four, had read his preliminary paper "Recherches sur la conductibilité galvanique des electrolytes," which, with van't Hoff's note, forms the basis of modern conceptions of electrolytic dissociation and of osmotic pressure, but the theories were not presented in final form by either author until 1887, when their papers appeared together in the first volume of the *Zeitschrift für physikalische Chemie.* The following passages are taken from these papers in the translation recently (1929) issued by the Alembic Club (*Reprint* No. 19). It will be recalled that in 1912 Arrhenius delivered the Silliman Lectures at Yale, which were published under the title, *Theories of Solutions.* He received the Nobel Prize in 1903, and van't Hoff had received it in 1901.

THE ROLE OF OSMOTIC PRESSURE IN THE ANALOGY BETWEEN SOLUTIONS AND GASES

By J. H. van't Hoff

In the course of an investigation which aimed chiefly at the acquisition of knowledge regarding the laws that regulate chemical eqilibrium in solution, it gradually appeared that there is a fundamental analogy, nay almost an identity, with gases, more especially in their physical aspect, if only in solutions we consider the so-called osmotic pressure instead of the ordinary gaseous pressure. This analogy will be made evident as far as possible in the following memoir, physical properties being first considered.

BOYLE'S LAW FOR DILUTE SOLUTIONS

The analogy between dilute solutions and gases immediately takes on a more quantitative form when we consider that in both cases a change of concentration has a similar influence on the pressure, the two magnitudes being in the two cases proportional to each other.

This proportionality, which for gases goes under the name of Boyle's Law, can be proved for osmotic pressure experimentally from known data, and also theoretically.

Experimental Proof. Determination of Osmotic Pressure at Different Concentrations. The following table contains Pfeffer's determinations of the osmotic pressure P in sugar solutions of concentration C at room temperature (13.2° to 16.1°):

C. *per cent*	*P.* *mm.*	*P/C*
1	535	535
2	1016	508
2.74	1518	554
4	2082	521
6	3075	513

The approximately constant quotients *P/C* point to an actual proportionality between pressure and concentration.

Experimental Proof. Physiological Comparison of Osmotic Pressures. The observations of de Vries may be cited in support, since it appears from them that equal changes in concentration of solutions of sugar, potassium nitrate, and potassium sulphate have the same influence on osmotic pressure. This investigator compared by a physiological method the osmotic pressure of the solutions with that of the contents of a plant cell, the protoplasmic membrane of which shrinks when it is brought into contact with solutions having a greater attraction for water. On systematic comparison of different solutions of these three substances with the same cells, three so-called isotonic liquids, *i.e.,* solutions of the same osmotic pressure, were obtained. Cells of another plant were now employed, and four isotonic series of this kind were thus obtained, which then showed a similar proportion for their various concentrations. The following table gives the concentrations in gram-molecules per litre:

Series	KNO_3	$C_{12}H_{22}O_{11}$	K_2SO_4	$KNO_3=1$	$C_{12}H_{22}O_{11}$	K_2SO_4
I	0.12	...	0.09	1	....	0.75
II	0.13	0.2	0.1	1	1.54	0.77
III	0.195	0.3	0.15	1	1.54	0.77
IV	0.26	0.4	....	1	1.54	....

Theoretical Proof. Although these experiments render the proportionality between osmotic pressure and concentration highly probable, the theoretical proof is a welcome addition, especially as it is almost self-evident. If we consider osmotic pressure to be of kinetic origin, that is, as arising from the impacts of dissolved molecules, we have to prove proportionality between the number of impacts in unit time and the number of impinging molecules in unit volume. The method of proof is thus exactly the same as that adopted for Boyle's Law in ideal gases. On the other hand if we see in osmotic pressure the effect of an attraction for water, its magnitude is obviously proportional to the number of attracting molecules in unit volume, with the proviso (which is fulfilled in sufficiently dilute solutions) that the dissolved molecules are without action on one another, and that each contributes on its own account a constant amount to this attractive action.

ON THE DISSOCIATION OF SUBSTANCES IN AQUEOUS SOLUTION

By Svante Arrhenius

In a memoir submitted to the Swedish Academy of Sciences on 14th October 1885 van't Hoff established both experimentally and theoretically the following very important generalisation of Avogadro's Law.

"La pression exercée par les gaz à une température déterminée si un même nombre de molécules en occupe un volume donné, est égale à la pression osmotique qu'exerce dans les mêmes circonstances la grande majorité des corps, dissous dans les liquides quelconques."

This law was proved by van't Hoff so conclusively that little doubt can exist as to its entire accuracy. There remained, however, a certain difficulty to be overcome, namely, that the law was only valid for the "great majority of substances," a very considerable number of the aqueous solutions examined forming exceptions, since they exert a much higher osmotic pressure than is required by the law.

When a gas shows a similar deviation from Avogadro's Law, the abnormality is explained by assuming that the gas is in a state of dissociation. A well-known example is afforded by the behaviour of chlorine, bromine, and iodine at high temperatures, these substances being regarded under the given conditions as split up into atoms. . . . .

Most of the properties of dilute salt solutions are of a so-called additive character. In other words, the numerical values of the properties may be regarded as the sum of the properties of the parts of the solution, *i.e.,* of the solvent and of the parts of the dissolved molecules, which in fact coincide with the ions. For example, the conductivity of a salt solution may be regarded as the sum of the conductivities of the solvent (generally zero), of the positive ion, and the negative ion. In most cases this can be tested by comparing two salts (*e.g.* of

K and Na) of one acid (*e.g.* HCl) with the corresponding salts of the same metals (K and Na) and another acid (*e.g.* HNO_3). Then the property of the first salt (KCl) minus the property of the second (NaCl) is equal to the property of the third salt (KNO_3) minus the property of the fourth ($NaNO_3$). This holds good in most cases for several properties, *e.g.* conductivity, lowering of the freezing point, refraction equivalent, heat of neutralisation, etc., which we shall briefly consider in the sequel, and finds its explanation in the almost complete dissociation of the great majority of salts into their ions. If a salt in aqueous solution is completely split into its ions, it follows naturally that the properties of this salt may in the main be expressed as the sum of the properties of the ions, since the ions are for the most part independent of each other, so that each ion has a characteristic value for the property, whatever be the oppositely charged ion with which it is associated. In the solutions actually investigated complete dissociation is probably never reached, and the above deduction is therefore not strictly accurate, but if we consider salts which are 80 or 90 per cent dissociated, as are almost without exception the salts of strong bases with strong acids, we shall in general commit no very great errors by calculating the values of the properties on the assumption that the salts are completely decomposed into their ions. According to the foregoing table this applies also to the strong bases and acids $Ba(OH)_2$, $Sr(OH)_2$, $Ca(OH)_2$, LiOH, NaOH, KOH, TlOH and HCl, HBr, HI, HNO_3, $HClO_3$, and $HClO_4$.

ERNEST HENRY STARLING

Ernest Henry Starling (1866-1927), for many years the Jodrell Professor of Physiology at University College, London, made pioneer studies upon the physiology of the circulation, the nature of lymph, and, in collaboration with Bayliss, a series of classical researches upon the hormone control of the pancreas. Undoubtedly his most important discovery, however, was the functional significance of the osmotic pressure of the proteins of the blood. It was he who first pointed out that since the capillaries were permeable to the blood crystalloids the effective osmotic pressure is that exerted by the serum proteins and that this is responsible for the absorption of fluid from the tissues. The following selection is taken from his original paper.[7]

[7] Starling, E. H. "Absorption by blood vessels." *Jour. Physiol.*, vol. 19, pp. 312-326, 1895 (pp. 322-325).

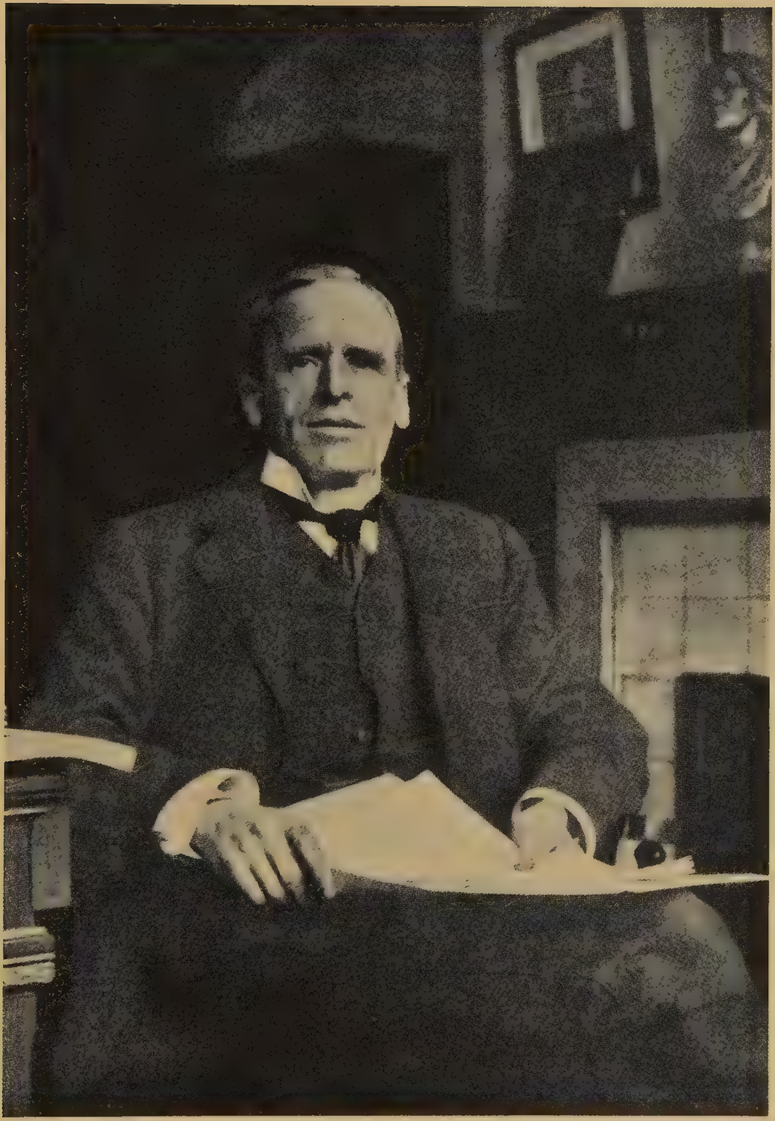


FIGURE 6. Ernest Henry Starling (1866-1927).

OSMOTIC PRESSURE OF SERUM PROTEIDS

In the limbs and connective tissues generally of the peripheral parts of the body, we have capillaries which are more or less impervious to proteids. As the blood passes under pressure through these capillaries, a certain amount of lymph is filtered through their walls, but in the process it loses the greater part of its proteids. We have therefore on one side of the capillary wall blood-plasma with 8% proteids, on the other side lymph containing 2 to 3% proteids. In this separation of proteid a certain amount of work must have been done, and if the proteids of serum are really analogous to the substance X of my illustration and possess an osmotic pressure, there must be a difference of osmotic pressure between intra- and extravascular fluids tending to a reabsorption of the latter. It becomes desirable to inquire whether the proteids of serum have any osmotic pressure and if so, what is the extent of this pressure.

To decide these points I have attempted to measure the osmotic pressure of the proteids in the serum directly. . . .

In all my experiments the fluid in the osmometer began to rise in the tube within two or three hours after the commencement of the experiment, and rose steadily for 3 or 4 days, the final height varying from 30 to 41 mm. Hg. I give here details of two of these experiments.

I. Jan. 27, 1896. Started an osmosis experiment; two osmometers (C and D) containing serum, while B contained a mixture of about ⅔ serum and ⅓ outer fluid. Outer fluid = 1% NaCl. Fluid forced up in the osmometers to heights varying from 3 to 6 inches. A few hours later the fluid in all osmometers had sunk about ¼ inch.

Jan. 29. Height of fluid in C and D = 13 inches = 32.5 cm.
Height of fluid in B = 9 inches = 22.5 cm.
Δ of outside fluid at beginning of exp. = —.605°C.
Δ of outside fluid at end of exp. = —.615°C.
Δ of serum in C and D at beginning = —.605°C.
Δ of serum in C and D at end = —.615°C.

(The outer fluid, being exposed to the air, concentrated by evaporation during the course of the experiment.)

II. Feb. 4, 1896. Three osmometers filled with serum.

A. Pressure raised to 60 cm. serum. This fell to 53 cm. in 30 mins. and to 50 cm. after 2 hrs.

B. Connected with Hg. manometer. Pressure started at 56 min.
C. Left open.

Feb. 5. (24 hrs. later.) At 11 a.m.
Height of A = 53 cm. (serum).
Height of B = 40 mm. Hg.
C had overflowed.

Feb. 5. At 4 p.m.
Height of A = 53 cm. serum.
Height of B = 40 mm. Hg.
Height of C = 15 cm. serum. Experiment stopped.

At beginning of experiment △ of serum = —.600°C.
At beginning of experiment △ of outer fluid (1.03% NaCl) = —.630°C.
At end of experiment △ of serum = —.635°C.
At end of experiment △ of outer fluid = —.635°C.
The serum contained 7.56% proteids.

The importance of these measurements lies in the fact that, although the osmotic pressure of the proteids of the plasma is so insignificant, it is of an order of magnitude comparable to that of the capillary pressures; and whereas capillary pressure determines transudation, the osmotic pressure of the proteids of the serum determines absorption. Moreover, if we leave the frictional resistance of the capillary wall to the passage of fluid through it out of account, the osmotic attraction of the serum for the extravascular fluid will be proportional to the force expended in the production of this latter, so that, at any given time, there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids. With increased capillary pressure there must be increased transudation, until equilibrium is established at a somewhat higher point, when there is a more dilute fluid in the tissue-spaces and therefore a higher absorbing force to balance the increased capillary pressure. With diminished capillary pressure there will be an osmotic absorption of salt solution from the extravascular fluid, until this becomes richer in proteids; and the difference between its (proteid) osmotic pressure and that of the intravascular plasma is equal to the diminished capillary pressure.

Here then we have the balance of forces necessary to explain the accurate and speedy regulation of the quantity of circulating fluid. It is evident however that we cannot explain in this way the absorption of serum or other fluids rich in proteids from the serous cavities and connective tissues. I would point out however that we have as yet no sufficient evidence that such fluids are absorbed by the blood vessels. If we inject serum into the pleural cavity we find that it is absorbed very much more slowly than is a similar amount of salt solution. The absorption is indeed so slow that it is impossible to exclude the possibility that the whole of it has taken place through the lymphatics. In two experiments in which I made the limb œdematous with serum instead of salt solution, I could obtain no evidence of absorption of the œdema fluid by the blood vessels. Details of these experiments are given at the end of the table on page 316. The extreme slowness with which inflammatory exudations, *i.e.,* fluids rich in proteids, are absorbed in man, also tells against the absorption of these fluids being effected directly by the blood vessels. It is evident however that, if serum be diffused through the meshes of a tissue, the cells of the tissue will feed on the proteids of the serum. As the serum becomes in this way more dilute, its water and diffuseable constituents may be taken up by the blood vessels. So far as I know there is no physical process other than filtration by which the absorption of proteids by the blood vessels could be effected. Filtration is excluded by my experiments in the case of the connective tissues of the limbs and peripheral parts of the body, so that a proof that proteids are absorbed in these situations would point to an active intervention of the endothelial cells in the process. All the physiological facts however which are so far definitely ascertained can be explained by the physical processes mentioned in this paper.

JOHN SCOTT HALDANE

John Scott Haldane, a pioneer in the study of respiration with modern methods, is known also for his writings upon the philosophical implications of physiological thought. His apparatus for the analysis of the respiratory gases was first described in 1892;[8] this was followed in 1899 by a book on methods of gas analysis. His monograph *Respiration,* founded on his Silliman Lectures, was published in 1922.[9] In the preface of this work one finds his *confessio fidei* as a physiologist and as it is an admirable summary of the point of view which he has adopted in his philosophical writings[10] it is quoted here.

---

[8] Haldane, J. S. "A new form of apparatus for measuring the respiratory exchange of animals." *Jour. Physiol.,* vol. 18, pp. 419-430, 1892; *Methods of air analysis.* London: C. Griffin and Company, Ltd., 1899 (3rd ed., x+137 pp., 1920).

THE ORGANISM AS A WHOLE

About the middle of last century the younger physiologists broke away from the vitalistic traditions which had been handed down to them, and set about to investigate living organisms piece by piece, precisely as they would investigate the working of a complex mechanism. This method seemed to them to promise success, and was popularized by such masters of clear and forceful expression as Huxley. It is still the orthodox method of physiology, but the old confidence in it has steadily diminished in proportion as exact experimental investigation has shown that the various activities of a living organism cannot be interpreted in isolation from one another, since organic regulation dominates them. The keynote of this book is the organic regulation of breathing and its associated phenomena.

The mechanistic theory of life is now outworn and must soon take its place in history as a passing phase in the development of biology. But physiology will not go back to the vitalism which was threatening to strangle it, and from which it escaped last century. The real lesson of the movement of that time will never be lost.

The book belongs to a transition period, but the transition is forward and not backward. My treatment of the subject may possibly be looked on askance in some quarters as reactionary: for I have been largely influenced by the ideas and work of older physiologists. If, however, I have gone backward, it is only to pick up clues which had been temporarily lost; and all of these clues lead forward—forward to a new physiology which embodies what was really implicit in the old.

The leaders of the mechanistic movement of last century got rid of vitalism, but in doing so got rid of life itself. I have tried to paint a picture of the body as alive. Though the picture is imperfect, others will soon paint it more completely. The time has come for a far more clear realization of what life implies. The bondage of biology to the physical sciences has lasted more than half a century. It is now time for biology to take her rightful place as an exact independent science: to speak her own language, and not that of other sciences.

---

[9] Haldane, J. S. *Respiration.* New Haven: Yale University Press; London: Humphrey Milford, Oxford University Press, xviii+427 pp., 1922 (pp. vii, viii, ix).

[10] Haldane, J. S. *Mechanism, life and personality. An examination of the mechanistic theory of life and mind.* London: John Murray, vii+139 pp., 6 leaves, 1913. *The new physiology and other addresses.* London: Charles Griffin and Company, Ltd., vii+156 pp., 1919. *The sciences and philosophy. Gifford Lectures, University of Glasgow 1927 and 1928.* London: Hodder and Stoughton Limited, ix+344 pp., 1929.

The endeavour to represent the facts of physiology as if they would fit into the general scheme of a mechanistic biology has led, it seems to me, to the present estrangement between physiology and medicine. Since the time of Hippocrates the growth of scientific medicine has in reality been based on the study of the manner in which what he called the "nature" (*φύσις*) of the living body expresses itself in response to changes in environment, and reasserts itself in face of disturbance and injury. The underlying assumption is that organic regulation and maintenance represent something very real, and that only through the study of it can we recognise and interpret disturbance of health, and effectively aid maintenance or restoration of health. I have endeavoured to return to what seems to me the truly scientific Greek tradition, and to give it a form which is not only consistent with modern science and philosophy, but brings physiology and medicine into that close and special relation indicated by the common etymology of the words "physician" and "physiology."

Most of the investigations specially referred to in the book have been carried out on man. It was only by human experiments that the almost incredible delicacy of the regulation of breathing was discovered; and human experiments have revealed to us in other ways how rough many of the experiments on animals, or on "preparations" from the bodies of animals, have been. Organic regulation, with its all-important relations to practical medicine and surgery, was often entirely overlooked. I hope that the book may contribute towards establishing human physiology in its rightful place, which has been usurped too long by experiments on fragments of frogs and other animals, or on the mere superficial physical and chemical aspects of bodily activity.

LAWRENCE HENDERSON

LAWRENCE JOSEPH HENDERSON, Professor of Biological Chemistry at Harvard University, has, like Haldane, elucidated the bearing of physiology upon philosophy. His essay, *The order of nature,*[11] in which a plea is made for a teleological interpretation of vital functions, appeared in 1917. His numerous papers on the buffer systems of the blood culminated in 1928 in his Silliman Lectures in which he gives full description of a cartesian nomogram by means of which the many dependent variables in blood can be plotted accurately in two planes of space. Unfortunately this work[12], like that of Willard Gibbs[13], which ranks with it in significance, does not lend itself to quotation. Henderson, however, is well known in the scientific world for another, equally original study *The fitness of the environment.*[14] In this work he has set forth an important general principle in physiology, *viz.,* the relation of the properties of water in its various physical states to living phenomena. The following quotation will serve to indicate the nature of this far-reaching conception.

---

[11] Henderson, L. J. *The order of nature. An essay.* Cambridge: Harvard University Press, vi+234 pp., 1917.

THE FITNESS OF THE ENVIRONMENT

For the convenience of my readers the argument which has been developed in the course of the preceding pages is here re-stated in outline.

I. Fitness is a mutual or reciprocal relationship between the organism and the environment.
II. Life is a mechanism (from the point of view of physical science). Accordingly it must be—
    a. Complex (physically, chemically, physiologically).
    b. Durable, hence well regulated physico-chemically. This conclusion applies to—
        1. The organism.
        2. The Environment.
    c. Endowed with a metabolism. Hence there must be exchange with the environment of—
        1. Matter.
        2. Energy.
III. The primary constituents of the natural environment are—
    a. Water.
    b. Carbonic acid.
IV. In places where life is possible the primary constituents of the environment are necessarily and automatically formed in vast amounts by the cosmic process.

---

[12] Henderson, L. J. *Blood. A study in general physiology.* New Haven: Yale University Press, xix+397 pp., 1928.

[13] Gibbs, J. W. "On the equilibrium of heterogeneous substances." *Trans. Conn. Acad.,* vol. 3, pp. 108-248, 1875-76; pp. 343-524, 1877-78.

[14] Henderson, L. J. *The fitness of the environment.* (pp. 267-273.) By permission of the Macmillan Co., publishers.

V. Water, carbonic acid, and their constituent elements manifest great fitness for their biological rôle.

  a. Water possesses a great number of unique or very unusual properties, *e.g.* thermal properties, solvent power, dielectric constant, surface tension, which together result in maximal fitness in certain respects, *e.g.*, mobility, ubiquity, constancy of temperature and richness of the environment, richness of the organism in chemical constituents, variety of chemical processes, electrical phenomena, colloidal phenomena.
  b. Carbon dioxide possesses very unusual properties, *e.g.* magnitude of absorption coefficient, strength as acid, which together result in maximal fitness in certain respects, *e.g.* mobility, ubiquity, richness of the environment and organism in other elements and compounds, constancy of reaction, etc.
  c. Chemical compounds containing carbon, hydrogen, and oxygen possess unique properties, *e.g.* number, variety, complexity, activity, variety of chemical relations and reactions, heats of reaction, instability, etc., which together result in maximal fitness in certain respects, *e.g.* as sources of matter and energy for the processes of metabolism, as sources of complex structures, as the means of establishing complex functions, etc.

VI. Oceans are formed automatically in the cosmic process.

VII. The ocean possesses unique properties, *e.g.* mobility, richness in dissolved substances, durability, and stability of physico-chemical conditions, depending chiefly upon the properties of water and carbonic acid, which together result in maximal fitness in certain respects, *e.g.* as *milieu,* and as source of matter for the processes of metabolism, to moderate and equalize temperature, etc.

VIII. The physical and chemical properties which have been taken into consideration include nearly all those which are known to be of biological importance or which appear to be related to complexity, regulation, and metabolism.

IX. There are no other compounds which share more than a small part of the qualities of fitness of water and carbonic acid; no other elements which share those of carbon, hydrogen, and oxygen.

X. None of the characteristics of these substances is known to be unfit, or seriously inferior to the same characteristic in any other substance.

XI. Therefore the fitness of the environment is both real and unique. In drawing this final conclusion I mean to assert the following propositions:—

I. The fitness of the environment is one part of a reciprocal relationship of which the fitness of the organism is the other. This relationship is completely and perfectly reciprocal;[15] the one fitness is not less important than the other, nor less invariably a constituent of a particular case of biological fitness; it is not less frequently evident in the characteristics of water, carbonic acid, and the compounds of carbon, hydrogen, and oxygen than is fitness from adaptation in the characteristics of the organism.

II. The fitness of the environment results from characteristics which constitute a series of maxima—unique or nearly unique properties of water, carbonic acid, the compounds of carbon, hydrogen, and oxygen and the ocean—so numerous, so varied, so nearly complete among all things which are concerned in the problem that together they form certainly the greatest possible fitness. No other environment consisting of primary constituents made up of other known elements, or lacking water and carbonic acid, could possess a like number of fit characteristics or such highly fit characteristics, or in any manner such great fitness to promote complexity, durability, and active metabolism in the organic mechanism which we call life.

It must not be forgotten that the possibility of such conclusions depends upon the universal character of physics and chemistry. Out of the properties of universal matter and the characteristics of universal energy has arisen mechanism, as the expression of physico-chemical activity and the instrument of physico-chemical performance. Given matter, energy, and the resulting necessity that life shall be a mechanism, the conclusion follows that the atmosphere of solid bodies does actually provide the best of all possible environments for life.

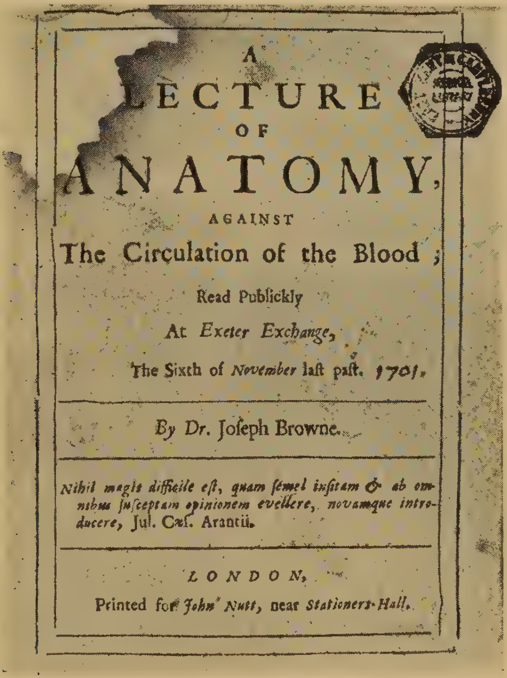
---

[15] This is not to be understood as an assertion that the relationship is symmetrical. The fact is that each organism fits its particular environment, while the environment in its most general and universal characteristics fits the most general and universal characteristics of the organic mechanism.

CHAPTER II

THE CIRCULATION OF THE BLOOD

THAT the blood exists under pressure in the arteries was well known in prehistoric times, and the pulse was recognised, probably by primitive man, as occurring synchronously with the heart beat. It is curious therefore that with the recognition of the veins—Seneca died by having his veins opened—the conception of the circulation of the blood was not immediately grasped. However, as James Young points out in the preface to his translation of Malpighi's *De pulmonibus* (see p. 62), many people, ill-acquainted with the history of science, are much too prone to assume that great ideas, when developed, might easily have been inferred from others long accepted. To Aristotle and Galen, both



A
LECTURE
OF
ANATOMY,
AGAINST
The Circulation of the Blood;
Read Publickly
At *Exeter Exchange*,
The Sixth of *November* laſt paſt. 1701.

By Dr. Joſeph Browne.

Nihil magis difficile eſt, quam ſemel inſitam & ab omnibus ſuſceptam opinionem evellere, novamque introducere, Jul. Cæſ. Arantii.

LONDON,
Printed for *John Nutt*, near *Stationers-Hall*.

FIGURE 7. The title-page of Joseph Browne's (*fl.* 1700) Lecture against the circulation of the blood, 1701.

of whom thought at length, and at times profoundly, about the movements of the blood, the pulse signified merely an ebbing and flowing along the selfsame channels. Harvey carefully studied their beliefs and in the *De motu cordis* appeals frequently to their authority, but he was able to emancipate himself from many, though not from all, of their doctrines. The passages from Galen given below are those actually quoted by Harvey in his book.

The growth of knowledge concerning the vascular system was painfully slow. Servetus, who mentioned his discovery of the pulmonary circulation casually in a theological treatise, remained unrecognised until nearly 150 years after he and his book had been burned at the stake. Harvey's announcement (1628) was greeted in many quarters with scepticism and derision, and as late as 1701 Joseph Browne delivered in London a lecture against the circulation of the blood (Fig. 7). We propose therefore to direct attention in this chapter chiefly to early developments in the subject. The next chapter will be devoted to more modern developments, especially to the capillary circulation to which many contributions have been made in recent years.

ARISTOTLE

Aristotle (384-322 B.C.) incorporated in his writings the beliefs of the Greeks concerning the functions of the body. Their contribution was one of observation and inference rather than of experiment and deduction. Aristotle had clearly made painstaking dissections of a very large number of vertebrate animals; he compared their organs and was aware of the more striking homologies of structure. His description of the heart is characteristic of his biological writings, but it shows the inevitable limitation of anatomical observation unaccompanied by experiment. The following passage[1] taken from the *De partibus animalium,* Book III, 4-5, has been selected to illustrate Aristotle's accuracy in anatomical description and also to show that, contrary to the inferences of certain recent writers, he certainly had no suspicion of the circulation of the blood. In the last paragraph below, he writes that the blood-vessels "become gradually smaller and smaller until at last their tubes are too fine to admit the blood." It would seem that this passage could never have been written had the idea of the circulation dawned upon him.

---

[1] From William Ogle's translation of the "De partibus" in *The works of Aristotle,* Oxford: Clarendon Press, vol. 5, 1912. The reader may also consult with profit A. Platt's excellent paper "Aristotle on the heart" in the *Studies in the history and method of science,* edited by Charles Singer, vol. 2, 1921, pp. 521-532; see also in the same volume Singer's paper "Greek biology and its relation to the rise of modern biology," pp. 1-101.

THE HEART

The apex of the heart is pointed and more solid than the rest of the organ. It lies against the breast, and entirely in the anterior part of the body, in order to prevent that region from getting chilled. For in all animals there is comparatively little flesh over the breast, whereas there is a more abundant covering of that substance on the posterior surface, so that the heat has in the back a sufficient amount of protection. In all animals but man the heart is placed in the centre of the pectoral region; but in man it inclines a little towards the left, so that it may counterbalance the chilliness of that side. For the left side is colder in man, as compared with the right, than in any other animal. It has been stated in an earlier treatise that even in fishes the heart holds the same position as in other animals; and the reason has been given why it appears not to do so. The apex of the heart, it is true, is in them turned towards the head, but this in fishes is the front aspect, for it is the direction in which their motion occurs.

The heart again is abundantly supplied with sinews, as might reasonably be expected. For the motions of the body commence from the heart, and are brought about by traction and relaxation. The heart therefore, which, as already said, is as it were a living creature inside its possessor, requires some such subservient and strengthening parts.

In no animals does the heart contain a bone, certainly in none of those that we have ourselves inspected, with the exception of the horse and a certain kind of ox. In these exceptional cases the heart, owing to its large bulk, is provided with a bone as a support; just as the bones serve as supports for the body generally.

In animals of great size the heart has three cavities; in smaller animals it has two; and in all has at least one, for, as already stated, there must be some place in the heart to serve as a receptacle for the first blood; which, as has been mentioned more than once, is formed in this organ. But inasmuch as the main blood-vessels are two in number, namely the so-called great vessel and the aorta, each of which is the origin of other vessels; inasmuch, moreover, as these two vessels present differences, hereafter to be discussed, when compared with each other, it is of advantage that they also shall themselves have distinct origins. This advantage will be obtained if each side have its own blood, and the blood of one side be kept separate from that of the other. For this reason the heart, whenever it is possible, has two receptacles. And this possibility exists in the case of large animals, for in them the heart, as the body generally, is of large size. Again it is still better that there shall be three cavities, so that the middle and odd one may serve as a centre common to both sides. But this requires the heart to be of greater magnitude, so that it is only in the largest hearts that there are three cavities.

Of these three cavities it is the right that has the most abundant and the hottest blood, and this explains why the limbs also on the right side of the body are warmer than those on the left. The left cavity has the least blood of all, and the coldest; while in the middle cavity the blood, as regards quantity and heat, is intermediate to the other two, being however of purer quality than either. For it behoves the supreme part to be as tranquil as possible, and this tranquillity can be ensured by the blood being pure, and of moderate amount and warmth.

The heart is of large size in the hare, the deer, the mouse, the hyena, the ass, the leopard, the marten, and in pretty nearly all other animals that either are manifestly timorous, or betray their cowardice by their spitefulness.

What has been said of the heart as a whole is no less true of its cavities and of the blood-vessels; these also if of large size being cold. For just as a fire of equal size gives less heat in a large room than in a small one, so also does the heat in a large cavity or a large blood-vessel, that is in a large receptacle, have less effect than in a small one. Moreover, all hot bodies are cooled by motions external to themselves, and the more spacious the cavities and vessels are, the greater the amount of spirit they contain, and the more potent its action. Thus it is that no animal that has large cavities in its heart, or large blood-vessels, is ever fat, the vessels being indistinct and the cavities small in all or most fat animals.

As the blood-vessels advance, they become gradually smaller and smaller, until at last their tubes are too fine to admit the blood. This fluid can therefore no longer find its way through them, though they still give passage to the humour which we call sweat; and especially so when the body is heated, and the mouths of the small vessels are dilated. Instances, indeed, are not unknown of persons who in consequence of a cachectic state have secreted sweat that resembled blood, their body having become loose and flabby, and their blood watery, owing to the heat in the small vessels having been too scanty for its concoction. For, as was before said, every compound of earth and water—and both nutriment and blood are such—becomes thicker from concoction. The inability of the heat to effect concoction may be due either to its being absolutely small in amount, or to its being small in proportion to the quantity of food, when this has been taken in excess. This excess again may be of two kinds, either quantitative or qualitative; for all substances are not equally amenable to concoction.

The widest passages in the body are of all parts the most liable to hæmorrhage; so that bleeding occurs not infrequently from the nostrils, the gums, and the fundament, occasionally also from the mouth. Such hæmorrhages are of a passive kind, and not violent as are those from the windpipe.

GALEN

GALEN (131-201 A.D.), a young Asiatic Greek who received his medical education at Alexandria, settled early in life at Rome, and there, through industry and cunning, established himself as the foremost physician of the empire. He became the medical attendant of Marcus Aurelius and formed a lasting and intimate friendship with this remarkable man. It is recorded that on one occasion the Emperor sent Galen a message that he was leaving the next day for the North to oppose the German invaders, and that he wished his physician to accompany him. Galen, who was at the moment in the midst of his experiments on the spinal cord, replied that on the previous night Aesculapius had come to him and told him that he must not leave Rome. The Emperor accepted the plausible reply and Galen was allowed to continue with his experiments! He was the first in the history of biology to appeal to experiment for an answer to questions confronting him, and he may in consequence be referred to as the founder of experimental physiology. There is scarcely a branch of the subject which, for better or for worse, he did not touch. He wrote prolifically, and is said to have employed twelve scribes to record the details of his observations and experiments. The following passage[2] on the circulation is of special interest since, as already mentioned, it was the one which Harvey quoted in 1628. The words in brackets are the connecting links which Harvey used in the quotation.

ANASTOMOSES AND VALVES

There is generally a mutual anastomosis or joining of the arteries and veins, and they transfer blood and spirit equally from each other by invisible and very small passages. If the mouth of the pulmonary artery always stayed open and Nature had no way of closing it when necessary or of opening it again, the blood could not transfuse through these invisible and delicate pores in the arteries during the contraction of the thorax. All things are not equally attracted or expelled. Something light is more easily drawn in by the distention of the part, and pushed out in contraction than something heavy. Likewise anything is more quickly passed through a wide tube than through a narrow one. When the thorax contracts, the pulmonary veins, strongly compressed on all sides, quickly expel some of the spirits in them, and take some blood from these tiny mouths. This could never happen if blood could flow back into the heart through the large opening of the pulmonary artery. Thus, its return through this great hole being blocked, and being compressed on every side, some of it filters into the arteries through these small pores.

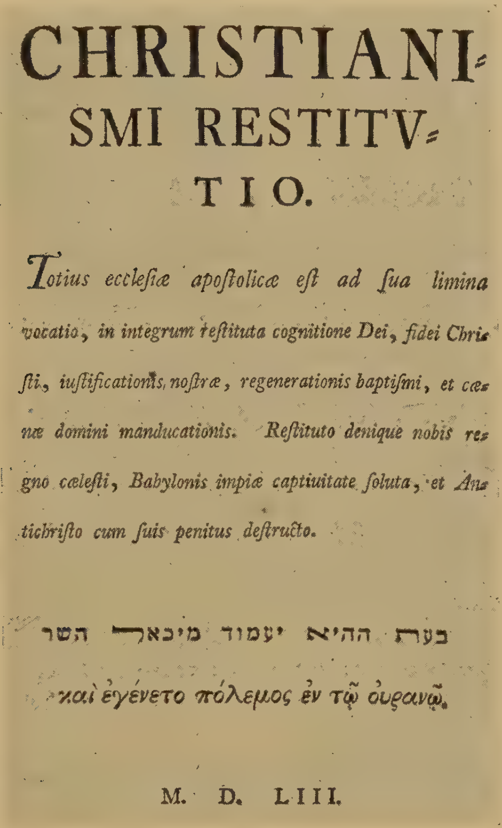
---

[2] Galen, *De Usu Partium.* See *Harvey De Motu Cordis,* 1628.

[Shortly after, in the next chapter:] The more powerfully the thorax contracts, squeezing the blood, the more tightly do these membranes, the sigmoid valves, close the opening, so that nothing flows back. [A little before in the 10th chapter:] Unless the valves be present, much difficulty would follow. The blood would follow this long course in vain, flowing in during the distention of the lungs and filling all the vessels in it, outwards during the constrictions, and tide-like, as Euripus, flow back and forth in a way not suited to the blood. This may not seem of much importance. Respiratory function, however, would suffer, and this would be of no little significance. [Again, a little later:] Another serious inconvenience would follow if our Maker had not provided these valves, the blood would move backwards during expirations. [So, in the 11th chapter, he concludes:] It seems that all these valves have a common function in preventing regurgitation, appropriate to both directions, one set leading away from the heart and preventing return by that route, the other leading into the heart and preventing escape from it. Nature never wished to fatigue the heart with useless work, neither bringing anything unnecessarily to it, nor taking anything unnecessarily from it. Thus there are four openings, two in each ventricle, one of which leads into the heart, the other out of it. [A bit farther on:] One of the blood-vessels fastened on the heart has a simple tunic, the other leading from it has a double tunic. [Galen is referring to the right ventricle, but the same things apply to the left.] The same cavity being provided for both of these, blood enters through the former and leaves through the latter.

MICHAEL SERVETUS

Michael Servetus (1509-1553), the discoverer of the pulmonary circulation, was a tragic figure of the sixteenth century who, had he been willing at his trial for heresy to substitute "Eternal Son of God" for "Son of the Eternal God," would have escaped the tortures of a slow and hideous death. At his burning the boughs were green, the wind in the wrong direction, and Calvin, his executioner, looked on relentlessly without a moment of pity or remorse. Servetus was a wandering Portuguese scholar, born of noble parentage at Villanueva de Sigena in Spain. He passed his early life in various university towns and spent a year (1532) in Paris as prosector with Vesalius in the laboratory of Guenther von



CHRISTIANISMI RESTITVTIO.

Totius eccleſiæ apoſtolicæ eſt ad ſua limina vocatio, in integrum reſtituta cognitione Dei, fidei Chriſti, iuſtificationis noſtræ, regenerationis baptiſmi, et cænæ domini manducationis. Reſtituto denique nobis regno cæleſti, Babylonis impiæ captiuitate ſoluta, et Antichriſto cum ſuis penitus deſtructo.

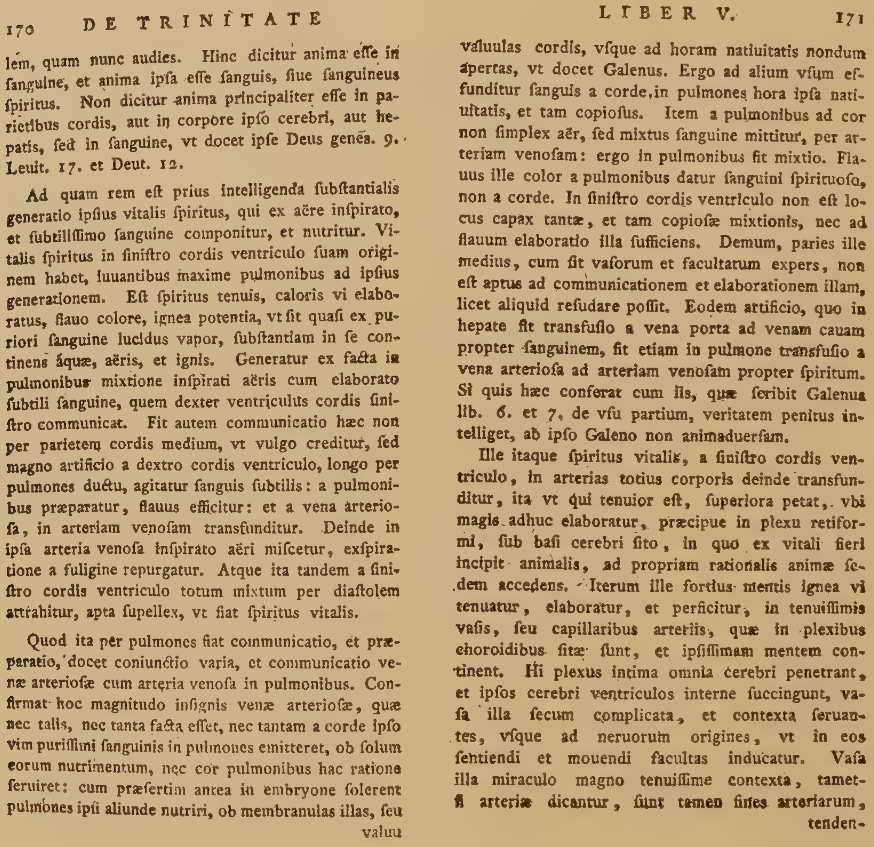
בעת ההיא יעמוד מיכאל השר

καὶ ἐγένετο πόλεμος ἐν τῷ οὐρανῷ.

M. D. LIII.

Figure 8. The title-page of the Murr reprint (1790) of the *Christianismi Restitutio* of Servetus, 1553. The reprint is now almost as scarce as the original.

Andernach. Guenther referred to him in his *Anatomicarum institutionum* (1539) as "Michael Villanovus distinguished by his literary acquirements of every kind and scarcely second to any in his knowledge of Galenical doctrine." It was probably at Paris that Servetus became convinced of the pulmonary circulation. However, he had early become drawn into theological controversy, and in 1531 had written anonymously an heretical tract entitled *De trinitatis erroribus.* The first mention of the pulmonary circulation, oddly enough, occurs in another theological work, *Christianismi restitutio* (1553), which was the cause of his conviction for heresy. As this book existed in manuscript before 1546, it accordingly establishes Servetus's priority over the claims of Realdus Columbus and others. Pages 170-171 on which the celebrated passage occurs are reproduced in fig. 9. The passage in question was first mentioned in 1695 by William Wotton,[3] to whom



170 DE TRINITATE

lem, quam nunc audies. Hinc dicitur anima eſſe in ſanguine, et anima ipſa eſſe ſanguis, ſiue ſanguineus ſpiritus. Non dicitur anima principaliter eſſe in parietibus cordis, aut in corpore ipſo cerebri, aut hepatis, ſed in ſanguine, vt docet ipſe Deus genes. 9. Leuit. 17. et Deut. 12.

Ad quam rem eſt prius intelligenda ſubſtantialis generatio ipſius vitalis ſpiritus, qui ex aëre inſpirato, et ſubtiliſſimo ſanguine componitur, et nutritur. Vitalis ſpiritus in ſiniſtro cordis ventriculo ſuam originem habet, iuuantibus maxime pulmonibus ad ipſius generationem. Eſt ſpiritus tenuis, caloris vi elaboratus, flauo colore, ignea potentia, vt ſit quaſi ex puriori ſanguine lucidus vapor, ſubſtantiam in ſe continens aquæ, aëris, et ignis. Generatur ex facta in pulmonibus mixtione inſpirati aëris cum elaborato ſubtili ſanguine, quem dexter ventriculus cordis ſiniſtro communicat. Fit autem communicatio hæc non per parietem cordis medium, vt vulgo creditur, ſed magno artificio a dextro cordis ventriculo, longo per pulmones ductu, agitatur ſanguis ſubtilis: a pulmonibus præparatur, flauus efficitur: et a vena arterioſa, in arteriam venoſam transfunditur. Deinde in ipſa arteria venoſa inſpirato aëri miſcetur, exſpiratione a fuligine repurgatur. Atque ita tandem a ſiniſtro cordis ventriculo totum mixtum per diaſtolem attrahitur, apta ſupellex, vt fiat ſpiritus vitalis.

Quod ita per pulmones fiat communicatio, et præparatio, docet coniunctio varia, et communicatio venæ arterioſæ cum arteria venoſa in pulmonibus. Confirmat hoc magnitudo inſignis venæ arterioſæ, quæ nec talis, nec tanta facta eſſet, nec tantam a corde ipſo vim puriſſimi ſanguinis in pulmones emitteret, ob ſolum eorum nutrimentum, nec cor pulmonibus hac ratione ſeruiret: cum præſertim antea in embryone ſolerent pulmones ipſi aliunde nutriri, ob membranulas illas, ſeu

valuu

LIBER V. 171

valuulas cordis, vſque ad horam natiuitatis nondum apertas, vt docet Galenus. Ergo ad alium vſum effunditur ſanguis a corde, in pulmones hora ipſa natiuitatis, et tam copioſus. Item a pulmonibus ad cor non ſimplex aër, ſed mixtus ſanguine mittitur, per arteriam venoſam: ergo in pulmonibus fit mixtio. Flauus ille color a pulmonibus datur ſanguini ſpirituoſo, non a corde. In ſiniſtro cordis ventriculo non eſt locus capax tantæ, et tam copioſæ mixtionis, nec ad flauum elaboratio illa ſufficiens. Demum, paries ille medius, cum ſit vaſorum et facultatum expers, non eſt aptus ad communicationem et elaborationem illam, licet aliquid reſudare poſſit. Eodem artificio, quo in hepate fit transfuſio a vena porta ad venam cauam propter ſanguinem, fit etiam in pulmone transfuſio a vena arterioſa ad arteriam venoſam propter ſpiritum. Si quis hæc conferat cum iis, quæ ſcribit Galenus lib. 6. et 7. de vſu partium, veritatem penitus intelliget, ab ipſo Galeno non animaduerſam.

Ille itaque ſpiritus vitalis, a ſiniſtro cordis ventriculo, in arterias totius corporis deinde transfunditur, ita vt qui tenuior eſt, ſuperiora petat, vbi magis adhuc elaboratur, præcipue in plexu retiformi, ſub baſi cerebri ſito, in quo ex vitali fieri incipit animalis, ad propriam rationalis animæ ſedem accedens. Iterum ille fortius mentis ignea vi tenuatur, elaboratur, et perficitur, in tenuiſſimis vaſis, ſeu capillaribus arteriis, quæ in plexibus choroidibus ſitæ ſunt, et ipſiſſimam mentem continent. Hi plexus intima omnia cerebri penetrant, et ipſos cerebri ventriculos interne ſuccingunt, vaſa illa ſecum complicata, et contexta ſeruantes, vſque ad neruorum origines, vt in eos ſentiendi et mouendi facultas inducatur. Vaſa illa miraculo magno tenuiſſime contexta, tametſi arteriæ dicantur, ſunt tamen fines arteriarum,

tenden-

FIGURE 9. The pages of Servetus's *Christianismi Restitutio,* 1553, on which occur the description of the pulmonary circulation (Murr reprint, 1790).

---

[3] *Reflections upon ancient and modern learning.* London: J. Leake, 1694. p. 211.

it had been pointed out by Mr. Charles Barnard, a surgeon of London. The translation is that of Willis.[4]

THE PULMONARY CIRCULATION

There is commonly said to be a threefold spirit in the body of man, derived from the substance of the three superior elements—a natural, a vital, and an animal spirit; there are, however, not really three, but only two distinct spirits. One of these, the first, characterized as *natural,* is communicated from the arteries to the veins by their anastomoses, and is primarily associated with the blood, the proper seat or home of which is the liver and veins. The second is the *vital* spirit, whose seat or dwelling-place is the heart and arteries. The third, the *animal* spirit, comparable to a ray of light, has its home in the brain and nerves. In each and all of these is the force—*energia*—of the one spirit and light of God comprised.

The heart is the first organ that lives, and, situated in the middle of the body, is the source of its heat. From the liver the heart receives the liquor, the material as it were of life, and in turn gives life to the source of the supply. The material of life is therefore derived from the liver; but, elaborated as you shall hear, by a most admirable process, it comes to pass that the life itself is in the blood—yea that the blood is the life, as God himself declares (Genes. ix.; Levit. xvii; Deut. xii).

Rightly to understand the question here, the first thing to be considered is the substantial generation of the vital spirit—a compound of the inspired air with the most subtle portion of the blood. The vital spirit has, therefore, its source in the left ventricle of the heart, the lungs aiding most essentially in its production. It is a fine attenuated spirit, elaborated by the power of heat, of a crimson colour and fiery potency—the lucid vapour as it were of the blood, substantially composed of water, air, and fire; for it is engendered, as said, by the mingling of the inspired air with the more subtle portion of the blood which the right ventricle of the heart communicates to the left. This communication, however, does not take place through the septum, partition or midwall of the heart, as commonly believed, but by another admirable contrivance, the blood being transmitted from the pulmonary artery to the pulmonary vein, by a lengthened passage through the lungs, in the course of which it is elaborated and becomes of a crimson colour. Mingled with the inspired air in this passage, and freed from fuliginous vapours by the act of expiration, the mixture being now complete in every respect, and the blood become fit dwelling-place of the vital spirit, it is finally attracted by the diastole, and reaches the left ventricle of the heart.

---

[4] Willis, R. *Servetus and Calvin.* London: Henry S. King, xvi+531+6 pp., 1877 (pp. 206-210). Those interested in the extraordinary details of the history of Servetus's book, only three copies of which are known to have escaped the flames, should consult the excellent notes in the *Bibliotheca Osleriana,* Nos. 839-896 (Oxford: Clarendon Press, 1929) and L. L. Mackall's "Servetus Notes" in *Contributions to Medical and Biological Research, Dedicated to Sir William Osler,* pp. 767-777, 1919.

Now that the communication and elaboration take place in the lungs in the manner described, we are assured by the conjunctions and communications of the pulmonary artery with the pulmonary vein. The great size of the pulmonary artery seems of itself to declare how the matter stands; for this vessel would neither have been of such a size as it is, nor would such a force of the purest blood have been sent through it to the lungs for their nutrition only; neither would the heart have supplied the lungs in such fashion, seeing as we do that the lungs in the fœtus are nourished from another source—those membranes or valves of the heart not coming into play until the hour of birth, as Galen teaches. The blood must consequently be poured in such large measure at the moment of birth from the heart to the lungs for another purpose than the nourishment of these organs. Moreover, it is not simply air, but air mingled with blood that is returned from the lungs to the heart by the pulmonary vein.

It is in the lungs, consequently, that the mixture [of the inspired air with the Blood] takes place, and it is in the lungs also, not in the heart, that the crimson colour of the blood is acquired. There is not indeed capacity or room enough in the left ventricle of the heart for so great and important an elaboration, neither does it seem competent to produce the crimson colour. To conclude, the septum or middle partition of the heart, seeing that it is without vessels and special properties, is not fitted to permit and accomplish the communication and elaboration in question, although it may be that some transudation takes place through it. It is by a mechanism similar to that by which the transfusion from the *vena portae* to the *vena cava* takes place in the liver, in respect of the blood, that the transfusion from the pulmonary artery to the pulmonary vein takes place in the lungs, in respect of the spirit.

The vital spirit (elaborated in the manner described) is at length transfused from the left ventricle of the heart to the arteries of the body at large, and in such a way that the more attenuated portion tends upwards, and undergoes further elaboration in the retiform plexus of vessels situated at the base of the brain, in which the *vital* begins to be changed into the *animal* spirit, reaching as it now does the proper seat of the rational soul. Here, still further sublimated and elaborated by the igneous power of the soul, the blood is distributed to those extremely minute vessels or capillary arteries composing the choroid plexus, which contain or are the seat of the soul itself. The arterial plexus penetrates even the most intimate part of the brain, its constituent vessels, interwoven in highly complex fashion, being distributed over the ventricles, and sent to the origins of the nerves which subserve the faculties of sensation and motion. Most wonderfully and delicately interwoven, these vessels, although spoken of as arteries, are really the terminations of arteries proceeding to the origins of nerves in the meninges. They are in truth a new kind of vessels; for, as in the transfusion from arteries to veins within the lungs we find a new kind of vessels proceeding from the arteries and veins, so, in the transfusion from arteries to nerves, is there a new kind of vessels produced from the arterial coats and the cerebral meninges.

HIERONYMUS FABRICIUS AB AQUAPENDENTE

Hieronymus Fabricius ab Aquapendente (1537-1619), a pupil of Fallopius, succeeded his master in 1565 in the chair of anatomy at Padua. There, for forty years until his death, he continued to attract innumerable pupils from all parts of the world, his lectures and anatomical demonstrations being second to none in Europe. In 1574 he discovered the valves in the veins and regularly demonstrated these structures to his pupils. In 1603 he published his description, but it is now known that he was not the first to see them. Giambattista Canano of Ferrara had observed them in 1545 and had communicated his discovery to Vesalius who, unfortunately for himself and for Canano, failed to recognize the observation and fancied that Canano was in error. The other claimants to priority have been discussed at length by K. J. Franklin in his attractive historical survey of the subject.[5] Fabricius himself failed to appreciate the physiological significance of these structures, for he still held the Galenical view that the veins carried crude blood to the tissues, and that the purpose of the valves was merely to prevent excess of blood from reaching the periphery. The following selection illustrates the vivid character of his anatomical writing.[6]

---

[5] Franklin, K. J. "Valves in veins: an historical survey." *Proc. Roy. Soc. Med.*, vol. 21 (Sect. Hist. Med.), pp. 1-33, 1927.

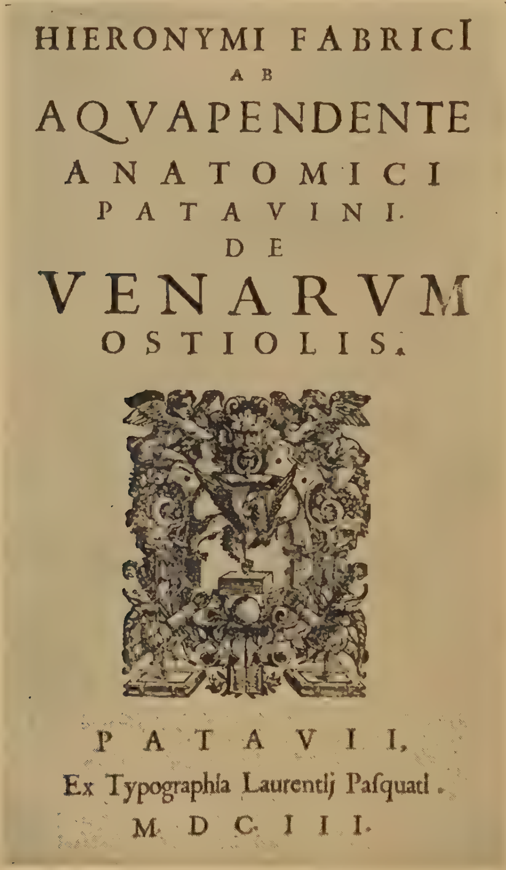
[6] Fabricius, H. *De venarum ostiolis.* Patavii: ex. typog. L. Pasquati, 23pp., 8 plates, fol., 1603. I am greatly indebted to Dr. K. J. Franklin of Oriel College, Oxford, for the excellent translation given below.

DOORLETS OF VEINS

By Hieronymus Fabricius

Anatomist of Padua

Doorlets of veins[7] is the name I give to some extremely delicate little membranes in the lumen of veins. They occur at intervals, singly or in pairs, especially in the limb veins. They open upwards in the direction of the main venous trunk, and are closed below, while, viewed from the outside, they resemble the swellings in the stem and small branches of plants.



HIERONYMI FABRICI
AB
AQVAPENDENTE
ANATOMICI
PATAVINI.
DE
VENARVM
OSTIOLIS.

PATAVII,
Ex Typographia Laurentij Paſquati.
M. D C. I I I.

Figure 10. The title-page of Fabricius's tract on the valves of the veins, 1603.

My theory is that Nature has formed them to delay the blood to some extent, and to prevent the whole mass of it flooding into the feet or hands and fingers, and collecting there. Two evils are thus avoided, namely, undernutrition of the upper parts of the limbs, and a permanently swollen condition of the hands and feet. Valves were made, therefore, to ensure a really fair all-round distribution of the blood for the nutrition of the various parts.

---

[7] Hereafter translated as *valves*.

A discussion of these valves must be preceded by a feeling of wonder at the way in which they have hitherto escaped the notice of Anatomists, both of our own and earlier generations; so much so that not only have they never been mentioned, but no one even set eye on them till 1574, when to my great delight I saw them in the course of my dissection. And this despite the fact that anatomy has claimed many distinguished men among its followers, men, moreover, whose research was conducted with great care and minuteness. But a certain amount of justification does exist for them in this case, for who would ever have thought that membranous valves could be found in the lumen of veins, especially as this lumen, designed for the passage of blood to the whole body, should be free for the free flow of the blood: just as in the case of the arteries, which are valveless, yet, in so far as they are channels for blood, are on the same footing as veins?

But a further justification can be advanced for the anatomists. All veins are not provided with valves. The vena cava, where it traverses the trunk of the body, the internal jugulars, and countless superficial veins in like manner, are destitute of them. On the other hand, a reasonable charge may be made against the earlier workers. Either they neglected to investigate the function of the valves, a matter, one would think, of primary importance, or else they failed to see them in their actual demonstration of veins. Nay more, when assistants pass a ligature round the limbs preparatory to blood-letting, valves are quite obviously noticeable in the arms and legs of the living subject. And, indeed, at intervals along the course of the veins certain knotty swellings are visible from the outside; these are caused by the valves. In some people, in fact, such as porters and peasants, they appear to swell up like varices: but here I must correct myself. It must be clearly stated that actual varices are due entirely to the dilatation of the valves and veins by too long retention and thickening of the blood at the valves; since in the absence of valves the veins would be expected to swell up and dilate uniformly throughout their length, differing thus from varices. From which begins to be visible one function of valves, namely, a strengthening action on the veins *per se.* For as in cases of varix, with valvular incompetence or rupture as an expected finding, one always sees a greater or lesser degree of venous dilatation, one can doubtless say with safety that the Supreme Artificer made valves to prevent venous distension. Venous distention and dilatation would, moreover, have occurred readily had the veins been of a membraneous texture, and that uniformly thin. And if they were to dilate, not only would the excessive accumulation of blood in them cause damage to themselves and the surrounding parts, and a swelling be caused, as has been known to occur in cases of limb varix. There would also be a more or less defective nutrition of the parts above with the blood rushing in force, say, to a site of venous dilatation, and collected, as it were, in a pool. Arteries, on the other hand, had no need of valves, either to prevent distension—the thickness and strength of their coat suffices—or to delay the blood—an ebb and flow of blood goes on continuously within them. But let us, if you will, consider the number, form, structure, site, distance, et cetera, of valves. It was certainly necessary to make valves in the limb veins either of large or medium calibre—not the small ones—in order, no doubt, to slow the blood flow everywhere to an extent compatible with sufficient time being given for each small part to make use of the nourishment provided. Otherwise the whole mass of blood, owing to the slope of the limbs, would flood into their extremities, and collect there, causing a swelling of these lower parts, and wasting of the parts above. That the blood flow is slowed by the valves, evident even without this from their actual construction, can be tested by anyone either in the exposed veins of the cadaver, or in the living subject if he passes a ligature round the limbs as in blood-letting. For if one tries to exert pressure on the blood, or to push it along by rubbing from above downwards, one will clearly see it held up and delayed by the valves. This indeed was the way in which I was led to an observation of such nature.

WILLIAM HARVEY

William Harvey (1578-1657), the discoverer of the circulation of the blood, was born in Folkestone; after attending Gonville and Caius College, Cambridge, he went to Padua (1598) and obtained there in 1602 the degree of doctor of physic. While at Padua Harvey came under the influence of Fabricius ab Aquapendente, the Professor of Anatomy. As we have seen in the previous passage, Fabricius had observed the valves in the veins as early as 1574. He frequently demonstrated these structures before his pupils and it is possible that Fabricius in this way sowed in the mind of the young Harvey the ideas which, a few years later, were to make his name immortal. When Harvey came to describe the circulation, one of the most important steps in his argument was the existence of valves so placed in the veins as to cause the blood to flow towards the heart. It has therefore seemed fitting to select from Harvey's book the chapter in which he discusses the venous return.

The story of the discovery of the circulation has been frequently told and it need not be repeated here. The subject, however, is one of very great fascination and scarcely a year passes in which some new light is not thrown upon Harvey or the circumstances of his work. He announced his discovery on April 17th, 1616—a week before Shakespeare's death—at his Lumleian Lecture to the College of Physicians in London. His lecture notes used at that time are still in existence, and in 1886 were carefully reproduced in facsimile.[8] The celebrated note relating to the circulation has been translated as follows by Professor Charles Singer: "On account of the structure of the heart, William Harvey is of the opinion that the blood is constantly passed through the lungs into the aorta, as by two clacks of a water bellows to raise water. Moreover, on account of the action of a bandage on the vessels of the arm he is of the opinion that there is a transit of blood from the arteries to the veins. It is thus demonstrated that a perpetual motion of the blood in a circle is brought about by the beat of the heart. What shall we say? Is this for the purpose of nutrition? Or is it for the better preservation of the blood and of the members by imparting heat to them, the blood by turns losing heat as it warms the members, and gaining heat from the heart?" Harvey was not prevailed upon to publish his theory until 1628, when he was 50 years of age; then, from the press of a second-rate publisher of Frankfort in Germany, appeared that miserably printed little book of 72 pages, which described the greatest discovery in the annals of medicine.[9] The introduction of the experimental method into physiological science, for which Harvey was responsible, was no less significant than the discovery of the circulation.

---

[8] Harvey, W. *Prelectiones anatomiæ universalis, edited with an autotype reproduction of the original by a committee of the Royal College of Physicians of London.* London: J. and A. Churchill, viii+98 pp., 1886.

[9] Harvey, W. *Exercitatio anatomica de motu cordis et sanguinis in animalibus, Guilielmi Harvei Angli, Medici Regii, & Professoris Anatomiæ in Collegio Medicorum Londinensi.* Francofurti, Sumptibus Guilielmi Fitzeri, 1628. English translations have appeared at various times; the first in 1653 by an unknown translator was replete with inaccuracies; this was reprinted in 1673 without change. Robert Willis's translation, published in 1857 by the Sydenham Society (*The works of William Harvey, M.D.*), has been many times reprinted (1889, 1894, 1907), but his pompous style was out of keeping with the simple idiomatic Latin which Harvey used. A fresh translation has recently been made by Leake, in which the attempt has been made to preserve in English the simplicity and directness of Harvey's diction (*Exercitatio anatomica de motu cordis et sanguinis in animalibus, With an English translation by Chauncey D. Leake.* Springfield, Illinois: Baltimore, Maryland: Charles C. Thomas, 1928, 4 leaves, 74+153 pp.). It is from this translation that the present selection has been made. For bibliographical information of unfailing accuracy concerning Harvey and the discovery of the circulation, one is referred to the *Bibliotheca Osleriana,* Nos. 692-918 (Oxford: Clarendon Press, 1929) and to G. L. Keynes's *A Bibliography of the writings of William Harvey* (Cambridge: University Press, 1928, 67 pp.).

CHAPTER XIII

THE THIRD PROPOSITION IS PROVEN, AND THE CIRCULATION OF THE BLOOD IS DEMONSTRATED FROM IT

So far we have considered the amount of blood flowing through the heart and lungs in the body cavity, and similarly from the arteries to the veins in the periphery. It remains for us to discuss how blood from the extremities gets back to the heart through the veins, and whether or not these are the only vessels serving this purpose. This done we may consider the three basic propositions proving the circulation of the blood so well established, so plain and obvious, as to force belief.

This proposition will be perfectly clear from a consideration of the valves found in the venous cavities, from their functions, and from experiments demonstrable with them.

The celebrated anatomist, Heironymus Fabricius of Aquapendente, or, instead of him, Jacobus Sylvius, as Doctor Riolan wishes it, first described membranous valves in the veins, of sigmoid or semilunar shape, and being very delicate eminences on the inner lining of these vessels. They are placed differently in different individuals, but are attached to the sides of the veins, and they are directed upwards toward the main venous trunks. As there are usually two together, they face and touch each other, and their edges are so apt to join or close that they prevent anything from passing from the main trunks or larger veins to the smaller branches. They are so arranged that the horns of one set are opposite the hollow part of the preceding set, and so on alternately.

The discoverer of these valves and his followers did not rightly appreciate their function. It is not to prevent blood from falling by its weight into areas lower down, for there are some in the jugular vein which are directed downwards, and which prevent blood from being carried upwards. They are thus not always looking upwards, but more correctly, always towards the main venous trunks and the heart. Others as well as myself have sometimes found them in the milky veins and in the venous branches of the mesentery directed towards the vena cava and portal vein. To this may be added that there are none in the arteries, and that one may note that dogs, oxen, and all such animals have valves at the branches of the crural veins at the top of the sacrum, and in branches from the haunches, in which no such weight effect of an erect stature is to be feared.

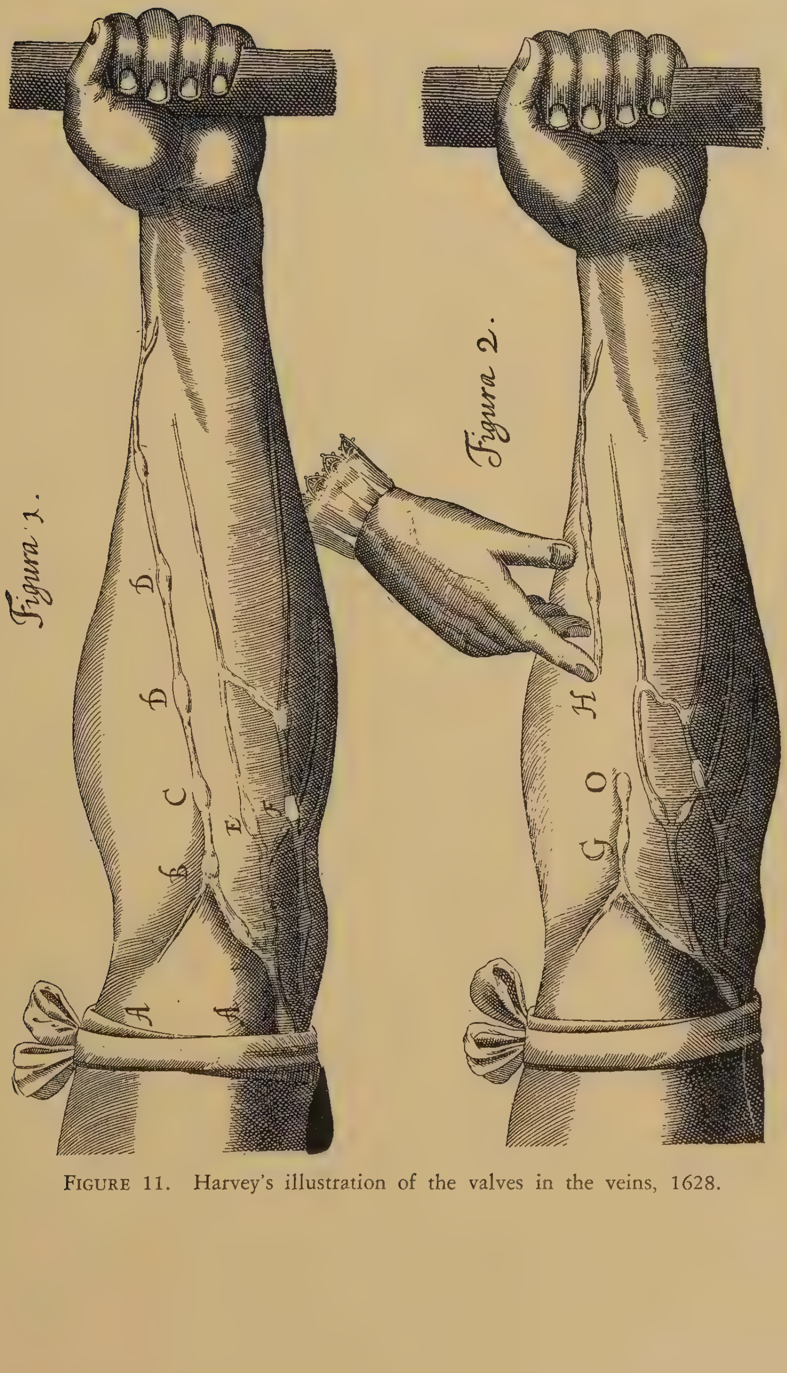


Figura 1.
D
D
C
B
E
F
A
A
Figura 2.
H
O
G

FIGURE 11. Harvey's illustration of the valves in the veins, 1628.

Nor, as some say, are the valves in the jugular veins to prevent apoplexy, since the head is more likely to be influenced by what flows into it through the carotid arteries. Nor are they present to keep blood in the smaller branches, not permitting it to flow entirely into the larger more open trunks, for they are placed where there are no branches at all, although I confess they are more frequently seen where there are branchings. Nor are they present for slowing the flow of blood from the center of the body, for it seems likely it would flow slowly enough anyway, as it would then be passed from larger to smaller branches, become separated from the source and mass, and be moved from warmer to cooler places.

The valves are present solely that blood may not move from the larger veins into the smaller ones lest it rupture or varicose them, and that it may not advance from the center of the body into the periphery through them, but rather from the extremities to the center. This latter movement is facilitated by these delicate valves, the contrary completely prevented. They are so situated that what may pass the horns of a set above is checked by those below, for whatever may slip past the edges of one set is caught on the convexity of those beyond, so it may not pass farther.

I have often noticed in dissecting veins, that no matter how much care I take, it is impossible to pass a probe from the main venous trunks very far into the smaller branches on account of the valvular obstructions. On the contrary it is very easy to push it in the opposite direction, from the branches toward the larger trunks. In many places a pair of valves are so placed that when raised they join in the middle of the vein, and their edges are so nicely united that one cannot perceive any crack along their junction. On the other hand, they yield to a probe introduced from without inwards and are easily released in the manner of flood-gates opposing a river flow. So they intercept, and when tightly closed, completely prevent in many places a flow of blood back from the heart and vena cava. They are so constituted that they can never permit blood to move in the veins from the heart upwards to the head, downwards toward the feet, or sidewise to the arms. They oppose any movement of blood from the larger veins toward the smaller ones, but they favor and facilitate a free and open route starting from the small veins and ending in the larger ones.

This fact may be more clearly shown by tying off an arm of a subject as if for blood-letting. There will appear at intervals (especially

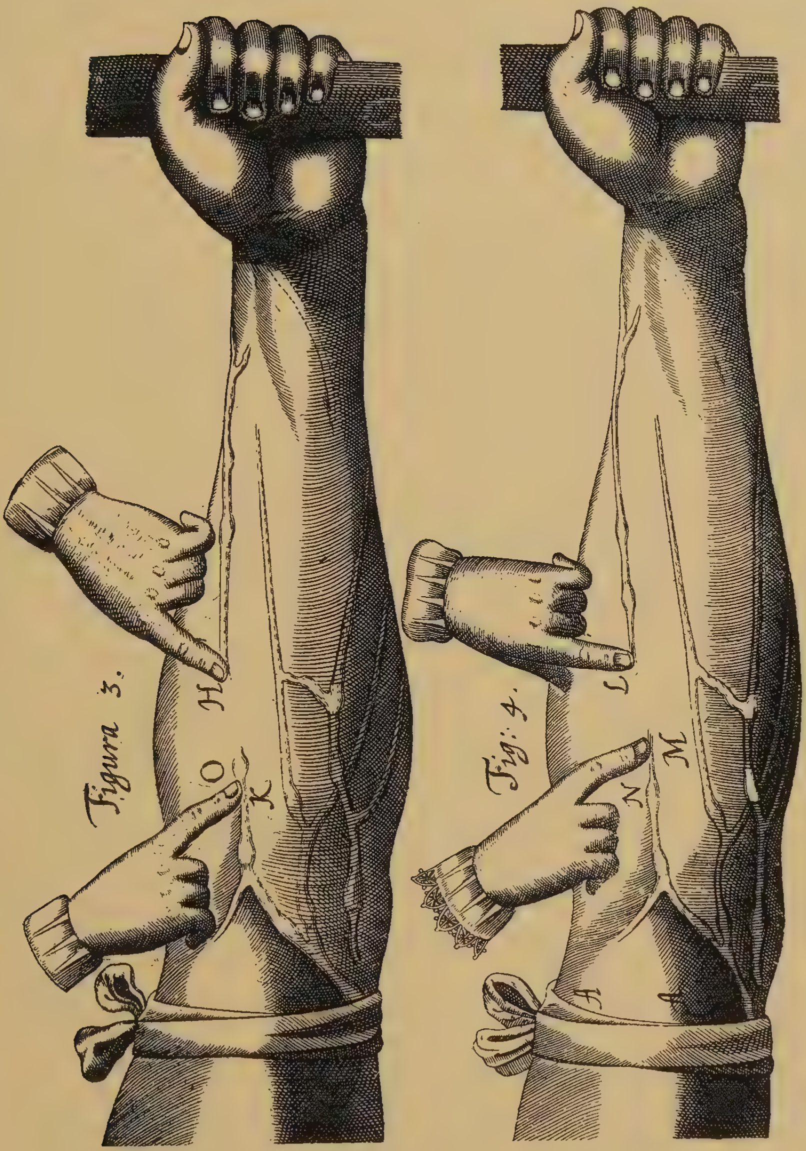


Figura 3.
H
O
K
Fig: 4.
L
M
N
A
A

FIGURE 11B.

in rustics) knots, or swellings, like nodules, not only where there is branching, but also where none occurs. These are caused by the valves, appearing thus on the surface of the hand and arm. If you will clear the blood away from a nodule or valve by pressing a thumb or finger below it, you will see that nothing can flow back, being entirely prevented by the valve, and that the part of the vein between the swelling and the finger, disappears, while above the swelling or valve it is well distended. Keeping the vein thus empty of blood, if you will press downwards against the valve, by a finger of the other hand on the distended upper portion, you will note that nothing can be forced through the valve. The greater effort you make the more the vein is distended toward the valve, but you will observe that it stays empty below it.

From many such experiments it is evident that the function of the valves in the veins is the same as that of the three sigmoid valves placed at the opening of the aorta and pulmonary artery, to prevent, when they are tightly closed, the reflux of blood passing over them.

Further, with the arm bound as before and the veins swollen, if you will press on a vein a little below a swelling or valve and then squeeze the blood upwards beyond the valve with another finger, you will see that this part of the vein stays empty, and that no back flow can occur through the valve. But as soon as the finger is removed, the vein is filled from below. Thus it is clearly evident that blood moves through the veins toward the heart, from the periphery inwards, and not in the opposite direction. The valves in some places, either because they do not completely close, or because they occur singly, do not seem adequate to block a flow of blood from the center, but the majority certainly do. At any rate, wherever they seem poorly made, they appear to be compensated for in some way, by the greater frequency or better action of the succeeding valves. So, as the veins are the wide open passages for returning blood to the heart, they are adequately prevented from distributing it from the heart.

Above all, note this. With the arm of your subject bound, the veins distended, and the nodes or valves prominent, apply your thumb to a vein a little below a valve so as to stop the blood coming up from the hand, and then with your finger press the blood from that part of the vein up past the valve, as was said before. Remove your thumb, and the vein at once fills up from below. Again compress with your thumb, and squeeze the blood out in the same way as before, and do this a thousand times as quickly as possible. By careful reckoning, of course, the quantity of blood forced up beyond the valve by a single compression may be estimated, and this multiplied by a thousand gives so much blood transmitted in this way through a single portion of the veins in a relatively short time, that without doubt you will be very easily convinced by the quickness of its passage of the circulation of the blood.

But you may say this experiment of mine violates natural conditions. Then if you will take as long a distance from the valve as possible, observing how quickly, on releasing your thumb, the blood wells up and fills the vein from below, I do not doubt but that you will be thoroughly convinced.

CHAPTER XIV

CONCLUSION OF THE DEMONSTRATION OF THE CIRCULATION OF THE BLOOD

Briefly let me now sum up and propose generally my idea of the circulation of the blood.

It has been shown by reason and experiment that blood by the beat of the ventricles flows through the lungs and heart and is pumped to the whole body. There it passes through pores in the flesh into the veins through which it returns from the periphery everywhere to the center, from the smaller veins into the larger ones, finally coming to the vena cava and right auricle. This occurs in such an amount, with such an outflow through the arteries, and such a reflux through the veins, that it cannot be supplied by the food consumed. It is also much more than is needed for nutrition. It must therefore be concluded that the blood in the animal body moves around in a circle continuously, and that the action or function of the heart is to accomplish this by pumping. This is the only reason for the motion and beat of the heart.

STEPHEN HALES

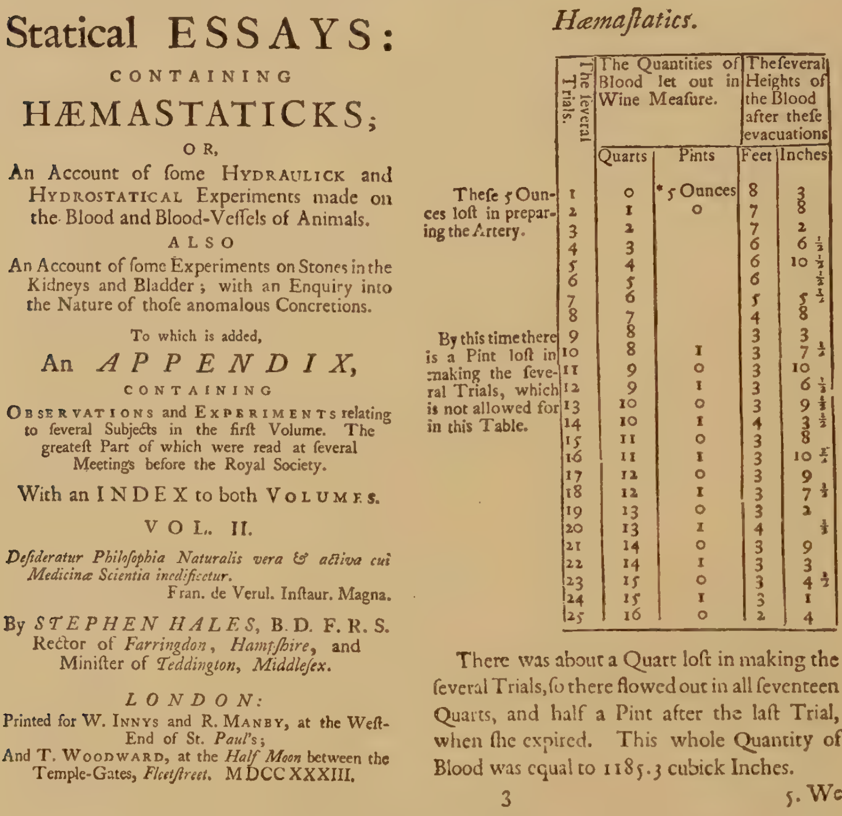
Stephen Hales (1677-1761), whose life is described in the following chapter, took the next important step after Harvey and Malpighi in elucidating the physiology of the circulation. The determination of blood pressure made it possible to calculate the work done by the heart, and to estimate for the first time the magnitude of the peripheral resistance. The following selection[10] is taken from his *Hæmastaticks* published in 1733.

---

[10] Hales, S. *Statical essays* [*vol. 2*]*: containing hæmastaticks; or, an account of some hydraulick and hydrostatical experiments made on the blood and blood-vessels of ani-*

EXPERIMENT III

1. In *December* I laid a common Field Gate on the Ground, with some Straw upon it, on which a white Mare was cast on her right Side, and in that Posture bound fast to the Gate; she was fourteen Hands and three Inches high; lean, tho' not to a great Degree, and about ten or twelve Years old. This and the above-mentioned Horse and Mare were to have been killed, as being unfit for Service.



Statical ESSAYS:
CONTAINING
HÆMASTATICKS;
OR,
An Account of ſome HYDRAULICK and HYDROSTATICAL Experiments made on the Blood and Blood-Veſſels of Animals.
ALSO
An Account of ſome Experiments on Stones in the Kidneys and Bladder; with an Enquiry into the Nature of thoſe anomalous Concretions.
To which is added,
An *APPENDIX*,
CONTAINING
OBSERVATIONS and EXPERIMENTS relating to ſeveral Subjects in the firſt Volume. The greateſt Part of which were read at ſeveral Meetings before the Royal Society.
With an INDEX to both VOLUMES.
VOL. II.
Deſideratur Philoſophia Naturalis vera & activa cui Medicinæ Scientia inedificetur.
Fran. de Verul. Inſtaur. Magna.
By *STEPHEN HALES*, B.D. F.R.S.
Rector of *Farringdon*, *Hampſhire*, and
Miniſter of *Teddington*, *Middleſex*.
LONDON:
Printed for W. INNYS and R. MANBY, at the Weſt-End of St. *Paul's*;
And T. WOODWARD, at the *Half Moon* between the Temple-Gates, *Fleetſtreet*. MDCCXXXIII.

Hæmaſtatics.

Theſe 5 Ounces loſt in preparing the Artery.

By this time there is a Pint loſt in making the ſeveral Trials, which is not allowed for in this Table.

The ſeveral Trials.	The Quantities of Blood let out in Wine Meaſure.		The ſeveral Heights of the Blood after theſe evacuations	
	Quarts	Pints	Feet	Inches
1	0	* 5 Ounces	8	3
2	1	0	7	8
3	2		7	2
4	3		6	6 ½
5	4		6	10 ½
6	5		6	½
7	6		5	5 ¼
8	7		4	8
9	8		3	3
10	8	1	3	7 ¼
11	9	0	3	10
12	9	1	3	6 ⅓
13	10	0	3	9 ⅓
14	10	1	4	3 ½
15	11	0	3	8
16	11	1	3	10 ¾
17	12	0	3	9
18	12	1	3	7 ½
19	13	0	3	2
20	13	1	4	⅓
21	14	0	3	9
22	14	1	3	3
23	15	0	3	4 ½
24	15	1	3	1
25	16	0	2	4

There was about a Quart loſt in making the ſeveral Trials, ſo there flowed out in all ſeventeen Quarts, and half a Pint after the laſt Trial, when ſhe expired. This whole Quantity of Blood was equal to 1185.3 cubick Inches.

3 5. We

FIGURE 12. The title-page of Hales's *Statistical Essays*, vol. 2, 1733, with one of his tables of blood-pressure.

2. Then laying open the left Jugular Vein, I fixed to that part of it which comes from the Head, a Glass Tube, which was four Feet, and two Inches long.

---

mals. . . . . London: W. Innys and R. Manby and T. Woodward, xxii pp., 13 leaves, 361 pp., 11 leaves, 1733 (pp. 13-17).

3. The Blood rose in it, in three or four Seconds of Time, about a Foot, and then was stationary for two or three Seconds; then in three or four Seconds more, it rose sometimes gradually, and sometimes with an unequally accelerated Motion nine Inches more, on small Strainings of the Mare: Then upon greater Strainings it rose about a Yard, and would subside five or six Inches: Then upon a larger Strain or Struggle of the Mare, it rose so high, as to flow a little out at the Top of the Tube; so that had the Tube been a few Inches higher, it would have risen probably to that Height.

4. When the Mare ceased to strain and struggle, the Blood subsided about eighteen or twenty Inches; so the Return of the Blood into the Vein was not hindred by the Valves; which I have also observed in other Parts where there are Valves, tho' sometimes they absolutely hinder the Return of any Fluid.

5. The Diameter of the Brass Pipe and Tube which were fixed to the Vein, were nearly one seventh of an Inch: The Diameter of the Jugular Vein about half an Inch.

6. Then laying bare the left Carotid Artery, I fixed to it towards the Heart the Brass Pipe, and to that the Wind-Pipe of a Goose; to the other End of which a Glass Tube was fixed, which was twelve Feet nine Inches long. The Design of using the Wind-Pipe was by its Pliancy to prevent the Inconveniencies that might happen when the Mare struggled; if the Tube had been immediately fixed to the Artery, without the Intervention of this pliant Pipe.

	The Several Trials	Cubic Inches let out	Perpendicular Height after each Evacuation	
			Feet	Inches
	1	70	9	6
	2	130	7	10
	3	190	7	6
	4	250	7	3
	5	310	6	5
	6	370	4	9
	7	430	3	9
	8	490	3	4½
* Deep Sighing raised the Blood.	9	550	2	9½
	10	610	3	2½
When the Force of the Blood was thus small, then faint Sweats came on.	11	670 }	*4 2	5 9½
	12	730	3	6
	13	790	3	5
Very faint.	14	820	2	0
Now expired.	15	833	2	5

7. There had been lost before the Tube was fixed to the Artery, about seventy cubick Inches of Blood. The Blood rose in the Tube in the same manner as in the Case of the two former Horses, till it reached to nine Feet six Inches Height. I then took away the Tube from the Artery, and let out by Measure sixty cubick Inches of Blood, and then immediately replaced the Tube to see how high the Blood would rise in it after each Evacuation; this was repeated several times, till the Mare expired, as follows, *viz.*

8. We may observe, that these three Horses all expired, when the perpendicular Height of the Blood in the Tube was about two Feet.

9. These 833 cubick Inches of Blood weight 28.89 Pounds, and are equal to fourteen Wine Quarts, the large Veins in the Body of the Mare were full of Blood, there was some also in the descending *Aorta,* and in both Ventricles and Auricles.

CHAPTER III

THE CAPILLARIES

THE continuity of ideas in a relatively limited field of physiological thought is nowhere more interestingly illustrated than in the development of knowledge concerning the capillaries. Through their walls the exchange of substances occurs between blood and tissue which makes possible the nutrition of the body. Before the existence of capillaries was established, the circulation of the blood was not completely proved and details of nutrition remained a mystery. Harvey probably suspected that minute vessels would be found connecting arteries with veins; but he did not commit himself and referred merely to an indefinite soakage of blood through the "Porosities of the tissue." Malpighi was the first to see and to describe the capillaries; Leeuwenhoek added to the knowledge of their structure, and Stephen Hales proved that "the small capillary vessels" became constricted and dilated under the action of various chemical substances. Those who believe that the problem of independent contractility of the capillaries has only been under discussion since the memorable papers of Lewis and Krogh in 1917-18, will turn with interest and profit to the acrimonious controversies which were waged over this very question by Whytt and his contemporaries in the 18th century, and by Black and Johannes Müller and others early in the 19th. The following passages, from the writers whom we have just mentioned, illustrate well the growth of knowledge in this singularly fascinating field. It is of course evident that many of the early writers did not distinguish between capillaries and the terminal arterioles.

MARCELLO MALPIGHI

Marcello Malpighi (1628-1694), Professor of Medicine at Bologna, carried out pioneer investigations in many fields of biological thought. He is usually referred to as the first histologist, but in addition to this he contributed fundamentally to botany, embryology, zoology and pathology, taking full advantage of the newly invented microscope. While an undergraduate at Bologna he came under the influence of Bartolommeo Massari, an ardent follower of the new learning whom Malpighi eventually succeeded in the Chair of Medicine. Massari gathered some of his older pupils into an informal club which met at his house. Malpighi soon joined their number and it is recorded that they discussed with enthusiasm the new discovery of Harvey and many other physiological problems, such as the functions of the lacteals, muscular movement, etc. Undoubtedly it was at this time that Malpighi became fired with the desire to learn more about the circulation. His unusual ability was almost at once apparent to his colleagues, and in 1656 one finds him in the Chair of Medicine at Bologna; in 1658 in the Chair of Theoretical Medicine (Physiology) at Pisa; and in 1662 in the Chair of Medicine at Messina. Eventually, however, he returned (1666) to his native town to resume duties as Professor of Medicine. While at Pisa Malpighi had formed a close friendship with Borelli and in 1661 addressed to him his two memorable letters on the lungs. After Harvey's discovery had been announced, it was thought that the blood, on passing into the lungs, became diffusely distributed within the porous parenchyma and the existence of microscopic channels between the two sides of the circulation had not been suspected. Malpighi studied the lung of a dog with the microscope, and proved in his first letter that the wind-pipe terminates in many small dilated air vessels; as Foster points out, he thus for the first time supplied the correct anatomical basis of respiratory exchange. In the second letter, from which quotation is made below,[11] he studied the lungs of frogs and beheld within them the small channels connecting arteries with veins which are now known as the capillaries.

EPISTLE II.—ABOUT THE LUNGS

And now, most famous man, I will handle the matter more closely. There were two things which, in my epistle about observations on the lungs, I left as doubtful and to be investigated with more exact study.

(1) The first was what may be the network described therein, where certain bladders and sinuses are bound together in a certain way in the lungs.

(2) The other was whether the vessels of the lungs are connected by mutual anastomosis, or gape into the common substance of the lungs and sinuses.

The solution of these problems may prepare the way for greater things and will place the operations of nature more clearly before the eyes. For the unloosing of these knots I have destroyed almost the whole race of frogs, which does not happen in that savage Batrachomyomachia of Homer. For in the anatomy of frogs, which, by favour of

---

[11] Malpighi, M. *De pulmonibus. Observationes anatomicæ.* Bologna, 1661. The first edition is an exceedingly rare book, no copy being known in England, and the editor has not seen one. Thomas Bartholin attacked Malpighi in a tract entitled *De pulmonum substantia et motu diatribe.* Hafniæ: Henricus Godianus, 3 l., 127 pp., 4 l., 1663. With this work Bartholin reproduces as an appendix Malpighi's two letters and an inferior reproduction of Malpighi's figures. The translation above is that recently given by James Young in the *Proc. Roy. Soc. Med.,* vol. 23, (Sect. Hist. Med.), pp. 1-14, 1929 (pp. 7, 8, 9, 10).

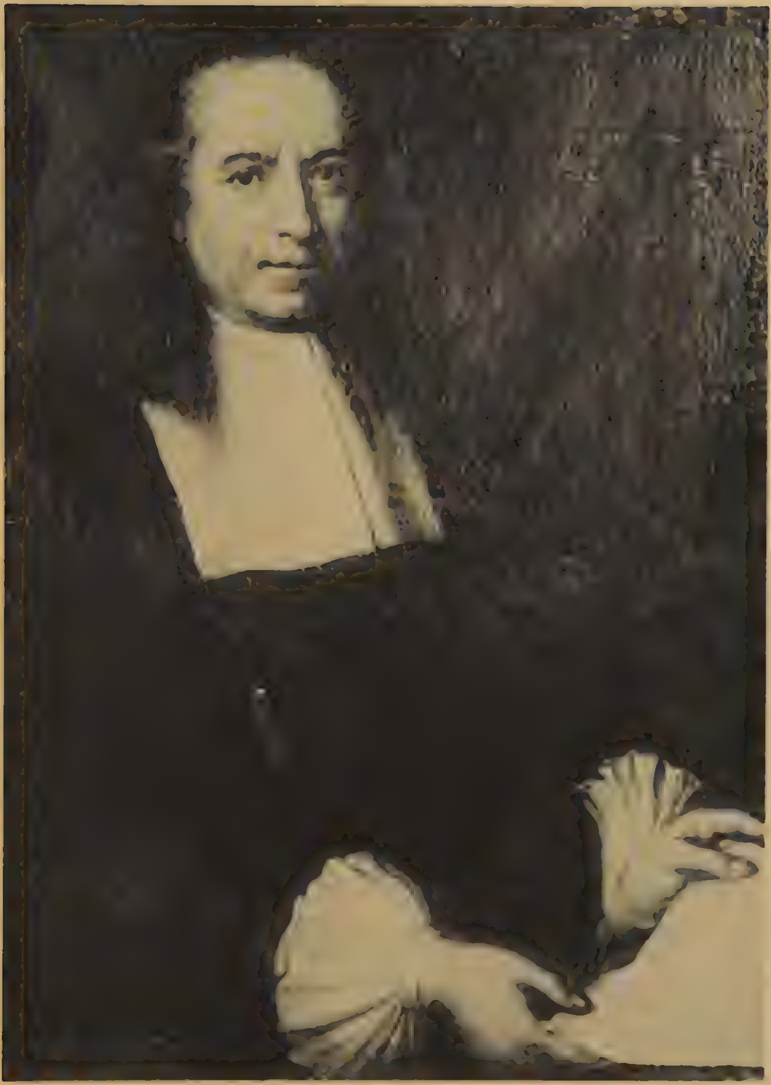


FIGURE 13. Marcello Malpighi (1628-1694). From an unassigned portrait in the Galleria Borghese at Rome, recently discovered by Prof. Capparoni to be Malpighi. The opened book is his *De Bombyce* (silk-worm) showing Plate III which served to identify the book and the portrait.

my very excellent colleague D. Carolo Fracassato, I had set on foot in order to become more certain about the membranous substance of the lungs, it happened to me to see such things that not undeservedly I can better make use of that (saying) of Homer for the present matter—

"I see with my eyes a work trusty and great."

Observation by means of the microscope will reveal more wonderful things than those viewed in regard to mere structure and connexion: for while the heart is still beating the contrary (i.e., in opposite directions in the different vessels) movement of the blood is observed in the vessels—though with difficulty—so that the circulation of the blood is clearly exposed. This is more clearly recognized in the mesentery and in the other greater veins contained in the abdomen.

Thus by this impulse the blood is driven in very small (streams) through the arteries like a flood into the several cells, one or other branch clearly passing through or ending there. Thus the blood, much divided, puts off its red colour, and, carried round in a winding way, is poured out on all sides till at length it may reach the walls, the angles, and the absorbing branches of the veins.

The power of the eye could not be extended further in the opened living animal, hence I had believed that this body of the blood breaks into the empty space, and is collected again by a gaping vessel and by the structure of the walls. The tortuous and diffused motion of the blood in divers directions, and its union at a determinate place offered a handle to this. But the dried lung of the frog made my belief dubious. This lung had, by chance, preserved the redness of the blood in (what afterwards proved to be) the smallest vessels, where by means of a more perfect lens, no more there met the eye the points forming the skin called Sagrino, but vessels mingled annularly. And, so great is the divarication of these vessels as they go out, here from a vein, there from an artery, that order is no longer preserved, but a network appears made up of the prolongations of both vessels. This network occupies not only the whole floor, but extends also to the walls, and is attached to the outgoing vessel, as I could see with greater difficulty but more abundantly in the oblong lung of a tortoise, which is similarly membranous and transparent. Here it was clear to sense that the blood flows away through the tortuous vessels, that it is not poured into spaces but always works through tubules, and is dispersed by the multiplex winding of the vessels. Nor is it a new practice of Nature to join together the extremities of vessels, since the same holds in the intestines and other parts; nay, what seems more wonderful, she joins the upper and the lower ends of veins to one another by visible anastomosis, as the most learned Falloppius has very well observed.

But in order that you may more easily get hold of what I have said, and follow it with your own sight, tie with a thread, just where it joins the heart, the projecting swollen lung of an opened frog while it is bathed on every side with abundant blood. This, when dried, will preserve the vessels turgid with blood. You will see this very well if you examine it by the microscope of one lens against the horizontal sun. Or you may institute another method of seeing these things. Place the lung on a crystal plate illuminated below through a tube by a lighted candle. To it bring a microscope of two lenses, and thus the vessels distributed in a ring-like fashion will be disclosed to you. By the same arrangement of the instruments and light, you will observe the movement of the blood through the vessels in question. You will yourself be able to contrive it by different degrees of light, which escape description by the pen. About the movement of the blood, however, one thing shows itself, worthy of your speculation. The auricle and the heart being ligatured, and thus deprived of motion and the impulse which might be derived from the heart into the connected vessels, the blood is still moved by the veins toward the heart so that it distends the vessels by its effort and copious flow. This lasts several hours. At the end, however, especially if it is exposed to the solar rays, it is agitated, not by the same continued motion, but, as if impelled by changing impulses, it advances and recedes fluctuating along the same way. This takes place when the heart and auricle are removed from the body.

From these things, therefore, as to the first problems to be solved, from analogy and the simplicity which Nature uses in all her operations, it can be inferred that that network which formerly I believed to be nervous in nature, mingled in the bladder and sinuses, is (really) a vessel carrying the body of blood thither or carrying it away. Also that, although in the lungs of perfect animals the vessels seem sometimes to gape and end in the midst of the network of rings, nevertheless, it is likely that, as in the cells of frogs and tortoises, that vessel is prolonged further into very small vessels in the form of a network, and these escape the senses on account of their exquisite smallness.

Also from these things can be solved with the greatest probability the question of the mutual union and anastomosis of the vessels. For if Nature turns the blood about in vessels, and combines the ends of the vessels in a network, it is likely that in other cases an anastomosis joins them; this is clearly recognized in the bladder of frogs swollen with urine, in which the above described motion of the blood is observed through the transparent vessels joined together by anastomosis, and not that those vessels have received that connexion and course which the veins or fibres mark out in the leaves of nearly all trees.

To what purpose all these things may be made, beyond those which I dealt with in the last letter concerning the pulmonary mixing of the blood, you yourself seemed to recognize readily, nor is the opinion to be lessened by your very famous device, because by your kindness you have entrusted me with elaborate letters in which you philosophised subtly by observing the strange portents of Nature in vegetables, when we wonder that apples hang from trunks not their own, and that by grafting of plants the processes have produced bastards in happy association with legitimates. We see that one and the same tree has assumed diverse fashions in its branches,—while here the hanging fruits please the taste by a grateful acidity, there they fulfill every desire by their nectar-like sweetness, and you furnish credibility to the truth at which you wondered when in Rome, that the vine and the jasmine had come forth from the bole of the Massilian apple. He who cultivated the gardens with a light inserted fork made these clever things with bigger branches, and he taught the unreluctant trees the bringing forth of divers things. About this matter Virgil in the Georgics fitly sang:—

"They ingraft the sprout from the alien tree
And teach it to grow from the moist inner bark."

I have put these few little observations into a letter that I might increase the things found out about the lungs. You will bring out the truth and dignity of these matters by your authority and contrivance. Meantime, apply yourself happily to philosophy, and may you go on to render me altogether happy by increasing a little my very unimportant thoughts of your writings "De Animalium Motu."

Farewell!

Bologna, 1661.

ANTONY VAN LEEUWENHOEK

Antony van Leeuwenhoek (1632-1723), the industrious and enthusiastic naturalist of Holland, was one of the first to use a microscope systematically for the study of living organisms and tissues. He possessed, during the course of his life, some 247 microscopes with 419 lenses ground largely by his own hand, and, on one occasion, presented twenty-six microscopes of his own design to the Royal Society of London. He sent more than 300 (308) letters to the Royal Society, a very large proportion of which were published in the *Philosophical Transactions,* and the original manuscripts of these interesting documents are still preserved in the archives of their library. The celebrated communication in which Leeuwenhoek described the capillary circulation was not actually published in the *Philosophical Transactions,* probably on account of its length and the fact that it was in Dutch. The following passage is taken from the English translation published in 1907 in vol. 1 of the *Opuscula Selecta Neerlandicorum de arte medica,* pp. 37-81.[12]

ANTONY VAN LEEUWENHOEK'S
65TH MISSIVE

Of the 7th of September 1688

Treating of

Two kinds of frogs. Of what parts their eggs consist. That tadpoles come out of these eggs. How these tadpoles are composed. The circulation of the blood in six different places in the head of these tadpoles. Continual sudden impulses given by the heart to the blood. Circulation of the blood in many places in the tail of the tadpole. What are called arteries and veins are continued blood-vessels. Arteries and veins crossing each other. The circulation takes place in the thinnest blood-vessels. The circulation of the blood in small and large frogs. How in an artery the blood came running back, and what was the cause of it. The circulation of the blood in a little fish, and thirty-four particular circulations in its tail, it also being shown very distinctly that arteries and veins are continued blood-vessels. In a part of our skin, the size of a nail, as many as a thousand circulations of the blood take place. The bodies that make the blood of fish red, are flat and oval. What gentlemen, amongst others, have seen the true circulation of the blood.

---

[12] Leeuwenhoek's letter on the capillary circulation is dated September 7th, 1688, and the original manuscript is at the Royal Society. It first appeared with the collected edition of his works which were issued in Dutch in five volumes between 1685 and 1718. It occurs in vol. 2 as the 65th "Missive" and bears the title "Den Waaragtigen Omloop des Bloeds, Ala mede dat de Arterian en Venæ gecontinueerde Bloed-Vaten zijn, Klaar voor de oogen gestelt."

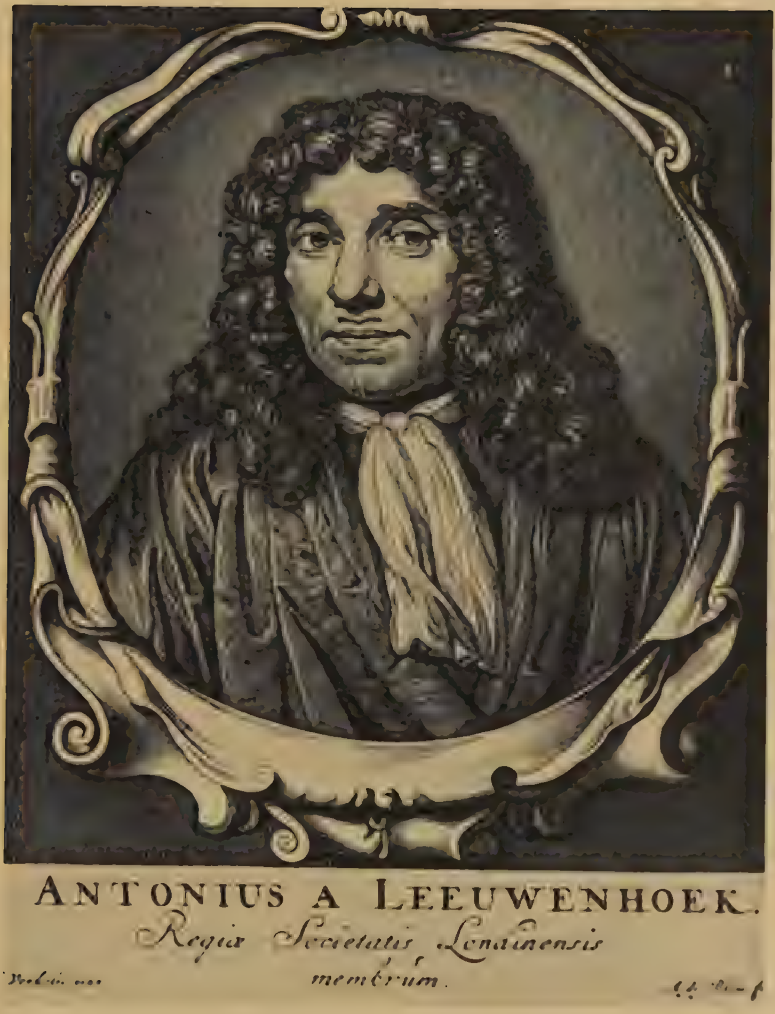

ANTONIUS A LEEUWENHOEK.
Regiæ Societatis Londinensis
membrum.

FIGURE 14. Antony van Leeuwenhoek (1632-1723) (from his *Epistolæ ad Societatem Regiam*, Leiden, 1719).

Most Honourable Gentlemen, etc.

My last most respectful letter to you was of the 24th. of last month, in which I treated of the sting of the gnat, namely, that this sting, taken out of its case, consists of four distinct stings.

Herewith I again send you some of my trifling observations.

In our country we have two species of frogs. The first, which we used to have in great abundance round about our town, is commonly called frog. Of late years, however, these frogs have been very rare, I suppose because our sluggish water-courses have lately been filled, as it were, with a kind of noxious little fish (hitherto unknown, so far as I am aware), called stickle-backs, which devoured the frogs when they were still tadpoles.

I was greatly pleased to see very distinctly the circulation of the blood [in the tadpole], which was driven on from the parts that were nearest to the body to those on the outside, thus causing an uninterrupted, very rapid circulation. This circulation was not regular in its movement, but at very short intervals it was continually brought about anew with sudden impulses, and before there was an other sudden impulse we might (in case we had not observed a continual increase in the rapidity) have thought that a stoppage in the circulation would follow. But scarcely had the blood begun to move more slowly, when there was again a sudden impulse of the blood, so that there was an uninterrupted current; and trying accurately to measure the very short time in which each impulse took place, I found that in the time wanted to count rapidly to a hundred, there were as many as a hundred sudden impulses. From this I concluded that as often as these sudden impulses occurred, the blood was driven from the heart.

In another place I saw that three of the thinnest arteries, each running in a curve, all met together in one point and there formed a blood-vessel or vein, and consequently this blood-vessel was as wide as the three arteries mentioned. These three distinct vessels with their somewhat circular course, in which the circulation took place, were so small that a grain of sand could have covered them.

Such blood vessels running across each other I often noticed before when I tried to discover the junction of arteries and veins in other animals, but I was quite certain that the return circuit of the blood does not take place in the large vessels, but in the smallest or thinnest, for if it were otherwise, I conclude that all the parts of the body could not be fed. And as these discoveries seemed inscrutable to me, I gave up my investigations on this head for some years. If now we see clearly with our eyes that the passing of the blood from the arteries into the veins, in the tadpoles, only takes place in such blood-vessels as are so thin that only one corpuscle can be driven through at one time, we may conclude that the same thing takes place in the same way in our bodies as well as in that of all animals. And this being so, it is impossible for us to discover the passing of the blood from the arteries into the veins in our bodies or that of other animals, first because a single globule of blood being in a vein, has no colour; secondly because the blood does not move in the blood-vessels when we make this investigation.

I have said before that the corpuscles or globules that make the blood red, are so small that ten hundred thousand of them are not so big as a grain of coarse sand, and so we can easily imagine how very small the blood-vessels are in which the circulation of the blood takes place.

The observations told here have not been made once, but they have been resumed repeatedly, giving me much pleasure, and every time on different tadpoles, and the result has almost always been the same. But it is remarkable that in the very small vessels mentioned above and placed furthest from the heart, as here at the end of the tail, the impulse was not by far so sudden and strong as in the vessels nearest to the heart. And though the uninterrupted current could be clearly observed, it could be distinctly seen that at each impulse from the heart the current was a little quicker.

When I looked along the length of the tail and at the thickest part of it, I could clearly see that on either side of the bone there was a large artery, through which the blood was carried to the extremity of the tail, and which on its way sent out several small branches.

When I looked at the part of the tail beside these arteries on the outside, I discovered there two large veins, which carried the blood back again to the heart, and moreover I saw that blood was driven into this large vein from several small veins. In short, I saw here the circulation of the blood to my perfect satisfaction, because there was nothing, though ever so slight, that caused me any doubt.

Also I observed the young frogs when they had changed from tadpoles into frogs and I also discovered in them a very large number of small blood-vessels which, continually running in curves, formed the vessels called arteries and veins, from which it was perfectly clear to

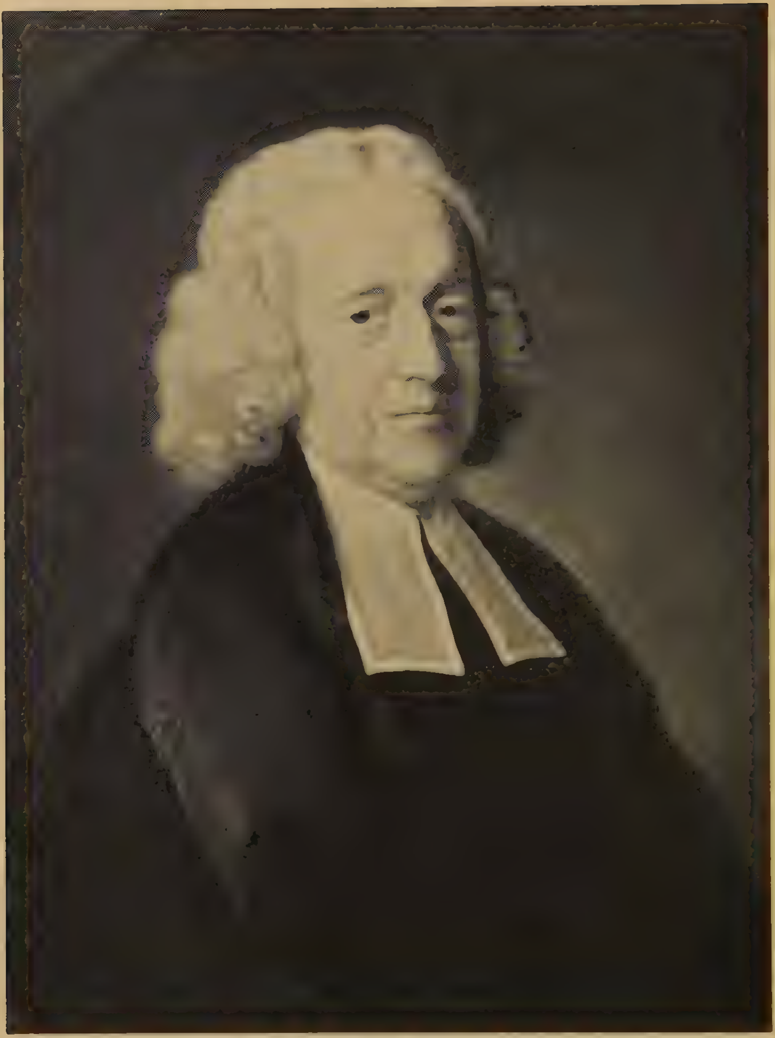


FIGURE 15. Stephen Hales (1677-1761) (from the portrait by Thomas Hudson in the National Portrait Gallery, London).

me that the arteries and veins are one and the same continuous blood-vessels. But I saw them clearest of all and most of all at the end of the projecting parts of the legs, which we may call fingers, and of which the frog has four on each fore-leg and five on each hind-leg.

These blood-vessels [*i.e.* capillaries], called "arteries and veins" (being nevertheless identical) were exceedingly numerous at the ends of these fingers, and each ran in a curve, which made it impossible to follow the particular course of each vessel. All these vessels were so small or thin that no more than one corpuscle could pass through it at a time. But when I examined these fingers about the first or second joint, I found the blood-vessels there, which we call arteries and veins, bigger, so big even that the blood in these vessels had a red colour.

STEPHEN HALES

Stephen Hales (1677-1761), the "perpetual curate" of the parish of Teddington in the county of Middlesex, occupied himself between his sermons with a series of observations on the mechanics of the circulation, which rank in importance with the studies of Harvey. Hales had been well grounded at Cambridge in the Newtonian physics and astronomy of the day, and in the laws of mechanics. The experiments described below were carried out alone and unassisted in a country parsonage after he left Cambridge in 1709, and they remained unpublished for a period of nearly twenty years. They were eventually issued as a second volume of his *Statical Essays* in 1733.[13] Hales had meanwhile, in 1717, become a Fellow of the Royal Society, before which body he frequently read papers. The recent fascinating biography of Hales by A.E. Clark-Kennedy (1929) may be recommended as one of the best lives of a scientific man written in recent years.[14] His account of determining the blood pressure by inserting a tube into the femoral artery of a mare, which he had "caused to be tied down," is well known. The experiments from which he inferred that changes occur in the diameter of the capillaries as a result of perfusion with certain chemical agents are less widely known. It is to be noted that he was not content to infer that capillary vessels existed, but that he actually made crucial observations of them in their living state under a microscope.

EXPERIMENT IX

1. I Slit open with a Pair of Scissors, from end to end, the Guts of a Dog, on that side which was opposite to the Insertion of the mesen-

---

[13] Hales, S. *Statical essays: Containing hæmastaticks; or, an account of some hydraulick and hydrostatical experiments made on the blood and blood-vessels of animals.* London: W. Innys and R. Manby, vol. 2, xxii+13 l.+361 pp.+11 l., 1733 (pp. 48-49; 56-58; 127-129; 133; 66-67; 70-72).

[14] Clark-Kennedy, A. E. *Stephen Hales, D.D., F.R.S. An Eighteenth Century Biography.* Cambridge, England: At the University Press, xii+256 pp., 1929.

terick Arteries and Veins; and having fixed a Tube 4½ Feet high to the descending *Aorta* a little below the Heart, I poured blood warm Water thro' a Funnel into the Tube, which descended thence into the *Aorta,* with a Force equal to that, with which the Blood is there impelled by the Heart: This Water passed off thro' the Orifices of innumerable small capillary Vessels, which were cut asunder thro' the whole Length of the slit Gut. But notwithstanding it was impelled with a Force equal to that of the arterial Blood in a live Dog, yet it did not spout out in little distinct Streams, but only seemed to ouze out at the very fine Orifices of the Arteries, in the same manner as the Blood does from the capillary Arteries of a Muscle cut transversely.

2. Having provided a Pendulum which beat Seconds, and pouring in thro' the Tube known Quantities of warm Water, I found that 342 cubic Inches of Water passed off in 400 Seconds or 6.6 minutes.

21. But the Resistance which the Blood meets with in those capillary Passages, may be greatly varied, either by the different Degrees of the Viscidity or Fluidity of the Blood, or by the several Degrees of Constriction or Relaxation of those fine Vessels; Instances of which may be seen in Experiments, XV, XVI, XVII, XVIII.

22. And as the State of the Blood or Bloodvessels are in these Respects continually varying from divers Causes, as Motion, Rest, Food, Evacuations, Heat, Cold, &c. so as probably never to be exactly the same, any two Minutes, during the whole Life of an Animal; so nature has wisely provided, that a considerable Variation in these, shall not greatly disturb the healthy State of the Animal.

23. We may make a pretty near Estimate of the Force of the Blood in the capillary Vessels in the following manner, *viz.* taking the Diameter of a Blood Globule to be as above 1/3240th part of an Inch; which *Leewenhoek* has observed to be of the same Size both in small and great Animals; and allowing these capillary Vessels to be a small Size larger than the Globules, which swim in and are carried along by *Serum* which surrounds them on all sides, we may therefore well suppose one of these Vessels to be double the Diameter of such a Globule, *viz.* 1/1620th part of an Inch or 0.00617, the Periphery therefore of this Vessel will be 0.0194, and its Area 0.0000298, which multipled by 80, the Number of Inches to which the Blood rose in the Tube when fixed to the Artery of the Dog Numb. 1, gives 0.0000298 parts of eighty cubic Inches of Blood or of 21416 Grains, equal to 1.997 Grains. But the Resistance of the Blood in the Veins of the same Dog being found

equal to six Inches Height or 1/12.5th part of eighty Inches, this 1/12.5th part being deducted out of 1.997 Grain, the Remainder 1.838 Grain is the Force with which the Blood would be impelled into such a Capillary by a Column of Blood of eighty Inches Height, supposing it were in a stagnant State; to which also must be added the Velocity which the Blood has acquired at its first Entrance in the capillary Vessel, which can be but small as appears by the great Resistance it meets with in the capillary Vessels, in this IXth Experiment, Numb. 18. whence we see both from Experiment and Calculation, that the Force of the Blood in these fine Capillaries can be but very little, and the longer such Capillaries are, the slower will the Motion of the Blood be in them.

3. I took a young Spaniel Dog which weighed twenty one Pounds, and as soon as he had bled to Death by having his jugular Veins cut, I immediately opened his *Thorax* and *Abdomen;* and having fixed a glass Tube, which was 4½ Feet high, to the descending *Aorta,* I then slit open his Guts from end to end the same manner as in *Experiment* IX; then having poured blood warm Water on them, and covered them with a folded Cloth dipped in the same Water, warm Water was poured into the Tunnel, which when it had subsided to a Mark on the lower Part of the glass Tunnel, eighteen cubic Inches of warm Water were immediately poured in, out of a Pot which held just that Quantity: The Time that it was running thro' the fine capillary Arteries was measured by a Pendulum that beat Seconds.

4. I first poured in seven Pots full of warm Water, the first of which passed off in fifty two Seconds, and the remaining six, gradually in less time, to the last which passed in forty six Seconds.

5. Then I poured in five Pots of common Brandy, or unrectify'd Spirit of Malt, the first of which was 68″ in passing, the last 72″.

6. Then I poured in a pot of warm Water which was 54″ in passing.

7. Hence we see that Brandy contracts the fine capillary Arteries of the Guts, and that Water soon relaxes them again, by diluting and carrying off the spirituous Part of Brandy, which as it is well known, not only contracts the Coats of the Blood-vessels, but also thickens the Blood and Humours, both which Effects contribute to the sudden Heating of the Blood, by much increasing thereby its Friction in the contracted capillary vessels; . . . .

5. I tried in like manner a strong Decoction of Oak Bark on another Dog, in which the preceding Pot of warm Water was 38″ in passing,

but the following six pots of Decoction so contracted the Vessels that the last of them was 136″ in passing.

8. When we view in a strong Light the Blood circulating in the Lungs of a Frog, we see the Arteries as they pass on, sending Branches, which spread like a fine Net-work over the Surface of each Vesicle; and on some of these Vesicles we may very plainly see, the Blood when it has pass'd over little more than half their Surfaces, to enter corresponding capillary Veins, which thence unite in large Trunks; but on the greatest part of the Vesicles, the extream capillary Arteries, reach to the Verges of the Vesicles, and there enter at right Angles the Veins, which run along the Limits of those Vesicles; which Veins laying on the inner Sides of those Vesicles they are not visible like the Arteries: But when in here and there a Place I have clearly seen those Veins, I have then also seen the extream capillary Arteries, pour at right Angles their single Globules, into those much larger Veins; agreeable to what I saw in the injected Vessels in *Exper.* XXI. *Numb.* 8.

9. Now by this means the Blood has a much freer Passage thro' the Lungs, where it is requisite for it to move with much greater Velocity than in other parts of the Body. Whereas in some if not all the Muscles, by entering the finer capillary Vessels at right Angles its Velocity is much retarded. I have observed that where a long capillary Artery branches off at an acute Angle, that there the Velocity of the Blood is many times greater, than where it branches off at right Angles, which plainly shews the great Degree of Retardation which the Blood suffers by its passing off at right Angles.

15. I shall hence take occasion to attempt an Estimate, tho' a very inaccurate one, of the Number of extream capillary Arteries in a Man's Body, in the following manner, *viz.* Supposing as is mentioned in *Exper.* VIII *Numb.* 8. that the Area of the transverse Section of the *Aorta* in Man, is 0.4187 Inch, and that the Length of the Cylinder of Blood, which is thrown out at each *Systole* of the left Ventricle, is 3.96 Inches; and the Area of a transverse Section of a fine extream capillary Artery being there set at 0.0000298 Inch: Then since equal Cylinders are as their Bases and Heights, the fine capillary Cylinder thrown out in each *Systole* of the Heart, will be 55639.98 Inches long: This Number multiplied by ten gives the Sum of that Column in 1/10 Inches, *viz.* 55639.98 each of which was the Space the Blood flowed in nine Seconds. But this Length being to pass the extream capillary Arteries of a Man, in 1/75th part of a Minute, that is in 1/8.88 of nine Seconds (the Time in which

the Blood moved 1/10th Inch in the Frog) tho' not with greater Velocity than in the Frog; therefore the Number of those extream Arteries in Man, must be proportionably increased by multiplying 556399.8 by 8.88, the Product is 494083, the astonishing Number of extream capillary Arteries. And if according to Dr. *Harvey* and Dr. *Lower,* double that Quantity of Blood be thrown out at each *Systole,* then the Number of extream capillary Arteries will also be double that Number, *viz.* 988166. And if the Velocity in the Lungs be 27.9 times greater as was found in *Exper.* IX. *Numb.* 6. then the Number of extream capillary Arteries there will be 3541713.

16. And how vastly more numerous are the many Branchings, Windings and Turnings of the Arteries and Veins, how innumerable the lymphatic Vessels and secretory Ducts? and these all adjusted and ranged, in the most exact Symetry and Order, to serve the several Purposes of the animal Oeconomy; *So curiously are we wrought, so fearfully and wonderfully are we made!*

ROBERT WHYTT

ROBERT WHYTT (1714-1766). The details of Whytt's life have been mentioned elsewhere. Here, we wish to direct attention to his little-known book, *Physiological essays,*[15] which appeared in Edinburgh in 1755, and passed through several editions. The work is chiefly controversial and is divided into two parts, the first entitled "An inquiry into the causes which promote the circulation of the fluids in the very small vessels of animals." Writers on the circulation in the 18th century fancied that peristaltic waves of contraction swept along the arterioles and capillaries, in this way assisting the heart. Whytt's consideration of this abandoned doctrine is critical and deserves to be recorded.

SECT. I

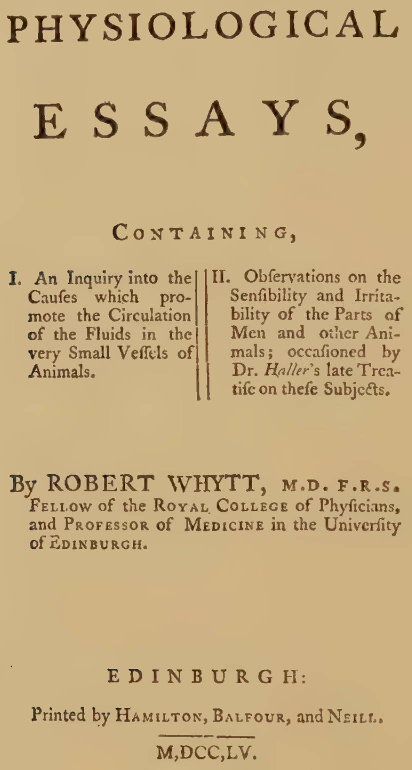
Of the force of the heart, contraction of the arteries, gravity and attraction of capillary tubes, considered as causes of the circulation of the fluids in the small vessels of animals.

The principal cause which propells the blood thro' the body, is, without doubt, the contraction of the heart: let us, then, first, inquire how far this may be supposed sufficient to account for the motion of the fluids in the very small vessels of animals.

If the force with which the blood is thrown, by the left ventricle of the heart, into the *aorta,* be supposed equal to the pressure of a column of blood 90 inches high[16]; the *momentum* of this fluid in any artery will be found, by multiplying the *area* of the transverse section of that artery into 90, the height of that column of blood, whose pressure is supposed equal to the protrusive force of the heart: for the product gives the number of cubic inches or parts of a cubic inch of blood, whose weight is equal to the pressing power with which the blood is driven by the force of the heart into that artery.

---

[15] Whytt, R. *Physiological essays.* Edinburgh: Hamilton, Balfour, and Neill, vii+223 pp., 1755 (pp. 5-8 and 38-39).



PHYSIOLOGICAL

ESSAYS,

CONTAINING,

I. An Inquiry into the Cauſes which promote the Circulation of the Fluids in the very Small Veſſels of Animals.

II. Obſervations on the Senſibility and Irritability of the Parts of Men and other Animals; occaſioned by Dr. *Haller*'s late Treatiſe on theſe Subjects.

By ROBERT WHYTT, M.D. F.R.S.
FELLOW of the ROYAL COLLEGE of Phyſicians,
and PROFESSOR of MEDICINE in the Univerſity
of EDINBURGH.

EDINBURGH:
Printed by HAMILTON, BALFOUR, and NEILL.
M,DCC,LV.

FIGURE 16. The title-page of Whytt's *Physiological Essays,* 1755.

The diameter of a circulating red globule of blood, has been generally reckoned something less than 1/3000 part of an inch; but Dr. *Martine* has, from *Lewenhoeck's* and *Jurin's* later observations, shewn it to be

---

[16] Dr. *Hales,* from a variety of experiments made on horses, dogs, sheep, and other animals, thinks it probable, that the blood would rise seven feet and an half, or 90 inches, in a tube fixed into the carotid artery of a middle-sized man. Statical Essays, vol. 2. p. 40.

1/1933.5 part of an inch[17]; and *Lewenhoeck* has observed, that one of these globules is sometimes obliged, in passing thro' a very small capillary artery, to change its figure into an oblong spheroid, so that the diameter of such an artery may be supposed nearly equal to that of a red globule. If then, for the sake of more easy computation, we suppose the diameter of a red capillary artery to be equal to 1/2000 part of an inch, the *area* of its transverse section will be 0.000 000 196, and this multiplied by 90 gives 0.0000176 parts of a cubic inch of blood, which amounts to 0.00466 or 1/214 part of a grain; and is equal to the moment of the blood, arising from the force of the heart, in a capillary artery, whose diameter is 1/2000 part of an inch, upon the supposition that there were no loss of motion from friction, and that the areas of the transverse sections of all the capillary arteries in the human body were equal to that of the *aorta:* but since this is not the case, and the areas of the former greatly exceed that of the latter; the moment of the blood in a capillary red artery, will fall very much short of our computation.

SECT. II

That the vibratory motion of the small vessels of animals is the principal cause promoting the circulation of the fluids.

Having shewn the insufficiency of the powers already mentioned to account for the circulation of the fluids in the very small vessels of animals, we shall now proceed to explain what we imagine to be the principal cause of this circulation.

Altho', as has been observed above, the regular alternate pulsation of the arteries does not extend beyond the capillaries of the first order, except, perhaps, in places very near the heart; yet we are not to consider the serous, lymphatic, and other still smaller vessels, as unactive canals no ways contributing to promote the circulation of their different fluids: on the contrary, it seems highly probable, that these vessels are continually agitated with very small alternate contractions, to which the circulation in them is, in a great measure, owing.

---

[17] Medical Essays, vol. 2. art. vii.

ALBRECHT VON HALLER

Albrecht von Haller (1708-1777), poet, bibliographer and physiologist, exerted a profound influence on physiological thought during the 18th century, perhaps greater than that of any other individual. His *Elementa physiologiæ corporis humani* in 9 volumes is a vast and well-systematized storehouse of physiological knowledge, replete with citation and an incredible number of accurate references to literature. His little book on the circulation[18] is divided into two parts, the first containing 174 pages of deductions which are based upon the protocols of the observations collected in Part 2 (pp. 175-343). Haller's conclusion that the capillaries are without contractility was held as a dogma by all orthodox physiologists until 1917. The few daring spirits, such as Black, Philip and Rouget, who were bold enough to record observations at variance with Haller, were greeted by deaf ears. The following paragraph contains Haller's statement of his conclusions; they were based, as we must now admit, upon faulty and incomplete observations.

The contractile force of the arteries is generally considered to be the second cause of the circulation of the blood. Many writers thought that this force was equal to that of the heart and others thought it was even greater. It is quite commonly believed that the power of the heart is enough to send the blood to the smallest arteries and that the force of the arteries then sends it back through the veins. This is also the commonest explanation of the fact that veins do not pulsate. It is thought that venous blood maintains an even movement because it is impelled by the force of the heart and the arteries alternately. Indeed, in warm-blooded animals and in man, one finds that even the smallest arteries of the brain have red fibres capable of contraction and of causing constriction. Experiments have been made which prove this force. If an artery is tied, the part below the ligature still goes on sending the blood which it contains into the veins; if two ligatures are made the blood between them continues to flow into the contiguous veins. When the aorta is ossified the vena cava is filled with coagulated stagnant blood. These are but a few of the many experiments of this sort.

Although I have no intention of refuting these facts, I think it is my duty to relate what the study of anatomy and my own experiments have

---

[18] Haller, Albrecht von. *Deux mémoires sur le mouvement du sang, et sur les effets de la saignée; fondés sur des expériences faites sur des animaux.* Lausanne: Marc-Mic. Bousquet and Comp., viii+343 pp., 1756 (pp. 136-139).

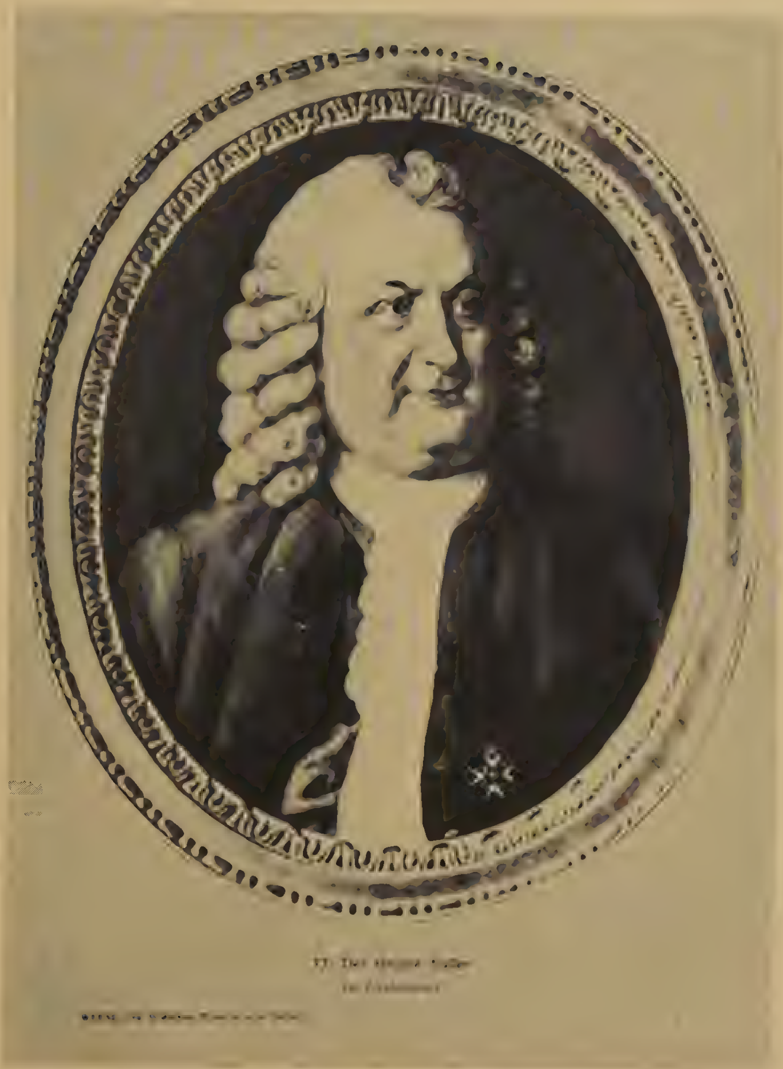
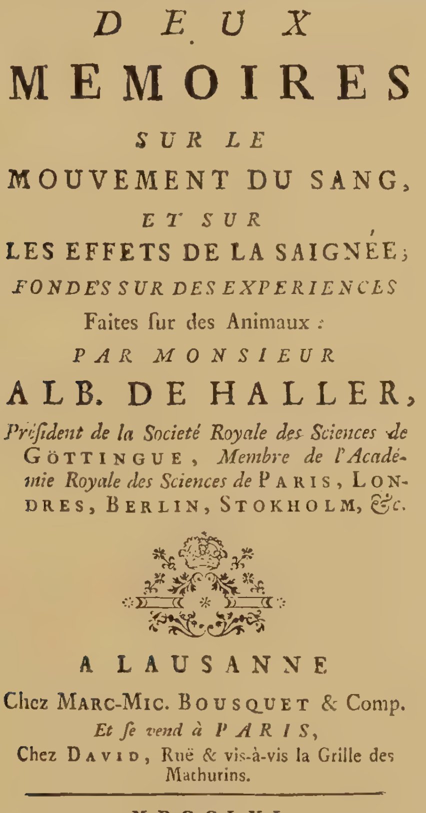


FIGURE 17. Albrecht von Haller (1708-1777). From Sigmund Freudenberger's portrait of 1773, considered by Weese, his iconographer, to be the best of all Haller's portraits (Weese, *Die Bildnisse Albrecht von Hallers.* Bern, 1909, p. 49).

taught me on this subject. In the first place, frogs' arteries appear to me to lack contractility at all times, either when studying the perfect equality of their diameter in a state of inanition and repletion, or the fact that the bitterest poison does not cause them to contract in the smallest degree; or when examining their composition, which is very much akin to that of cellular tissue, and contains no fleshy fibres; or finally, considering that they have no pulse, since it appears to follow that vessels which do not dilate do not contract either. Frogs' arteries and veins when touched with spirit of nitre undergo no change, nor do they contract even when the poison alters the blood in the vessels, giving it an earthy colour and muddy consistency. It is almost impossible to conclude anything from the inanition of the blood-vessels. In frogs



DEUX
MEMOIRES
SUR LE
MOUVEMENT DU SANG,
ET SUR
LES EFFETS DE LA SAIGNÉE;
FONDE'S SUR DES EXPERIENCES
Faites ſur des Animaux:
PAR MONSIEUR
ALB. DE HALLER,
Préſident de la Societé Royale des Sciences de GÖTTINGUE, *Membre de l'Académie Royale des Sciences de* PARIS, LONDRES, BERLIN, STOKHOLM, *&c.*

A LAUSANNE
Chez MARC-MIC. BOUSQUET & Comp.
Et ſe vend à PARIS,
Chez DAVID, Ruë & vis-à-vis la Grille des Mathurins.

MDCCLVI.

FIGURE 18. The title-page of Haller's *Deux mémoires sur le mouvement du sang,* 1756, in which are recorded his observations on the capillaries.

the arteries are often quite empty and after bleeding, below ligatures and in various other circumstances, corpuscles of blood can be seen gradually leaving the artery until it is quite white and empty. These vessels can even become so empty that there is not a single drop of blood left in them. But I have satisfied myself by several experiments that the blood-corpuscles move about in the arteries even though the arteries do not contract, and independently of the heart's force. In an artery which is nearly empty numbers of corpuscles can be seen to advance into the artery, hesitate there and retreat and finally disappear, without the slightest movement of the vessels, or diminution in the diameter of the artery after the blood has left it, being detectable through the most powerful microscope.

JOHANNES MÜLLER

JOHANNES MÜLLER (1801-1858), whose life is described elsewhere, was deeply interested in almost every phase of physiology, and his celebrated *Handbuch der Physiologie der Menschen* is, like Haller's *Elementa Physiologiæ,* a vast compendium of physiological knowledge of his day. The critical attitude which he adopts in the following passage[19] on the capillaries is highly characteristic of his logical habits of thought.

Contractility of the capillaries.—Many substances, such as those called astringents,—for example, alum,—seem to have the property of producing an approximation of the molecules of living animal matter,—a condensation of the matter,—and thus a contraction of the tissues which it forms. It is to this effect on the capillaries and small arteries that we must attribute the action of such astringents, and of cold, in arresting hemorrhage from wounds.

There can be little doubt but that the effect of cold and astringents on the animal textures is much greater during life, for it is only during life that the peculiar state of the skin, called "cutis anserina," can be produced. If the "cutis anserina" arose simply from the blood being repelled from the surface, so as to leave the capillaries less turgid, the skin collapsed, and the follicles consequently more prominent, it would be produced by the same cause after death. It must, therefore, be dependent on a vital contractility of the skin; the follicles becoming more evident in consequence of the contraction of the surrounding skin. A similar contraction is produced in the prepuce by the action of cold, and in a still greater degree in the dartos. The vital insensible contractility here referred to is distinguishable from muscular contractility by the contraction of the part in which it is excited being gradual and feeble; moreover, muscular contractions are excited by the nervous stimulus under all circumstances, while this insensible contraction of the skin is not excited by its specific causes, such as cold and nervous affections, unless under such circumstances as at the same time determine a diminished flow of blood to the skin, which is probably dependent on some sympathetic influence on the heart's action; while all stimulants which induce a greater afflux of blood to the surface produce vascular turgescence, but not the phenomenon of cutis anserina. The insensible contractility displayed by the skin is probably possessed, in agreater or less degree, by all the soft parts which are organised; and there is no reason to suppose that the minute arteries and capillaries are not endued with it. Every stimulant, however, does not excite it. Thus the contraction of the small arteries and capillaries, which causes the arrest of hemorrhage in operations, is produced by the sudden action of specific influences,—such as cold; while other stimuli,—heat, for example,—might, by increasing the turgescence of the part, have quite the contrary effect. Wedemeyer states that no contraction is produced in the capillaries by the agency of galvanism, but that the blood becomes stagnated in them from coagulation taking place. In the small arteries, however, he perceived a distinct permanent contraction, which did not arise, he says, from the action of the acid developed at the positive pole, for it took place even when he applied the negative pole to the vessel. It might, however, in this case, be dependent on the action of the alkali developed at the negative pole.

---

[19] From Baly's English translation of Müller's *Handbuch* which appeared under the title of *Elements of physiology.* London: printed for Taylor and Walton. 2 vols., i-xxii+1-848 pp. (1838); xxii-xxxviii+8-48-1715+22 pp. (1842) (pp. 226-227).

Action of different substances on the capillaries.—Direct experiments to determine the action of different substances on the capillary vessels, by watching the changes produced by the application of these substances to the vessels of transparent parts, promised at first to increase considerably our knowledge of the action of the capillaries. But these experiments have left our knowledge of the subject in the greatest confusion. The most interesting observations are those of Thomson, Wilson, Hastings, Kaltenbrunner, Wedemeyer, and Koch. Two orders of changes are observed on the application of chemical agents to the small arteries, capillaries, and veins. In many instances,—for example, whenever common salt was applied,—dilatation of the capillaries ensued after a few minutes. In Wedemeyer's experiments, however, on the application of salt to the small arteries of the mesentery of the frog, contraction to the extent of 1/5th of their diameter was the first effect, and this was followed by great dilatation. The application of ammonia was observed by Thomson to be followed by contraction of the vessels, with diminished rapidity of the circulation; while Wedemeyer and Hastings found it produce dilation of the vessels with stagnation of the blood. Oesterreicher also observed dilatation follow the application of a weak solution of ammonia, while he found that concentrated matters produce contraction of the vessels, and at last stagnation of the blood. Alcohol, according to Hastings, produced contraction of the capillaries: hot water had the same effect in frogs; the application of ice was also followed by contraction. Hastings remarked that these substances frequently caused contraction first, and afterwards dilatation. From the application of tincture of opium, tartaric acid, very dilute muriatic acid and alcohol, Wedemeyer obtained no constant result. In two instances only did alcohol cause retardation of the circulation, without, however, having excited distinct contraction in the small arteries. When dilatation of the vessels is produced, the circulation is generally at the same time retarded. Thomson is the only physiologist who has observed acceleration as well as retardation of the circulation accompanying dilatation of the vessels; and this was after the application of common salt. In vessels in which the substance applied has produced contractions, the rate of the circulation also varies, being sometimes retarded, sometimes accelerated.

ALEXANDER PHILIP WILSON PHILIP

Alexander Philip Wilson Philip (circa 1770-1851?), physician and physiologist, was an erratic Scottish genius, who, despite a lucrative practice in London, carried out a series of important observations upon the physiology of the nervous system and the capillary circulation. He disappeared mysteriously from London in 1842 and is believed to have died abroad about 1851. Thackeray's Dr. Firmin in the *Adventures of Philip* is drawn from Philip and the unhappy ending of his life. The following passage indicates the character of his scientific observations.[20] It is to be noted that he had observed 'central' acceleration and inhibition of the heart as a result of stimuli applied directly to tissue of the nervous system.

---

[20] Philip, A. P. W. *An experimental inquiry into the laws of the vital functions,* 3rd edition. London: T. and G. Underwood, lv+339 pp., 1826 (pp. 80-81; 83-84; p. 100; pp. 72-73).

Exp. 30. A frog was rendered nearly insensible by having its back immersed in laudanum. A ligature was then thrown round the neck to prevent loss of blood, part of the cranium removed, the web of one of the hind legs brought before the microscope, and the circulation in it, which was rapid, observed. A strong infusion of tobacco was then applied to the brain, with the effect of at first rendering the circulation more rapid. In about half a minute it became more languid, and soon stopped altogether. On the infusion of tobacco being washed off, the circulation returned and regained considerable vigour. The tobacco was several times applied to the brain and washed off, with the same effects. It may be observed, that when the circulation in the web had almost ceased after the tobacco had been washed off, its velocity was immediately increased on applying spirit of wine to the brain.

The power of the blood-vessels, like that of the heart, is capable of being directly destroyed through the medium of the nervous system.

The author has often watched the capillaries from the commencement of inflammation to its greatest height, when the part is about wholly to lose its vital power, in the mesentery of a rabbit, the web of a frog's foot, and the fins of fishes, without perceiving the least tendency to this irregular motion when the part viewed was so applied to the microscope as not to compress any of its vessels.[21] When the circulation fails without any morbid distension of the vessels, the motion of the blood becomes irregular before it stops altogether; when it fails from morbid distension of the vessels, which gives rise to the phenomena of inflammation, this irregularity is not perceived, the motion of the blood gradually becomes slower, till it ceases altogether.

What are the simple results of the experiments related in this and the preceding chapter? The first set prove, that the power of the heart and vessels of circulation is independent of the brain and spinal marrow, for we find that the functions of the former organs continue after the latter are destroyed or removed, and that their removal is not attended with any immediate effect on the motions of the heart and vessels. The second set prove, that the action of the heart and vessels of circulation may be influenced by agents applied either to the brain or spinal marrow. It is as readily influenced by agents applied to the anterior part of the brain, as by those applied to the cervical part of the spinal marrow. This is what we should expect when we trace the origins of their nerves.

---

[21] An account of these experiments is published in the introduction to the author's Treatise on Symptomatic Fevers, and a plate given representing the state of the vessels in the different stages of inflammation. See also the last part of this Inquiry.

Exp. 47. The cervical part of the spine of a newly-dead rabbit was laid open, and a wire was repeatedly passed transversely through the spinal marrow, without being able at all to affect the motion of the heart; but on the wire being passed longitudinally, so as to bring it into contact with a larger portion of the spinal marrow, the motion of the heart was immediately accelerated. On the same principle, when the wire was made to wound many minute portions of the brain and spinal marrow in quick succession, the action of the heart was increased.

Exp. 19. The reader has seen that if the head and spinal marrow of a frog be removed, the heart continues to perform its function perfectly for many hours, nor does it seem at all immediately affected by their removal. But we find the effect very different when the most sudden and powerful agent is applied to them. If either the brain or spinal marrow be instantly crushed, the heart immediately feels it. The brain of a large frog was crushed by the blow of a hammer. The heart immediately performed a few quick and weak contractions. It then lay quite still for about half a minute. After this its beating returned, but it supported the circulation very imperfectly. In ten minutes its vigour was so far restored, that it again supported the circulation with freedom, but with less force than before the destruction of the brain. An instrument was then introduced under the heart, and after ascertaining that this had produced no change on its action, the spinal marrow was crushed by one blow, as the brain had been. The heart again beat quickly and feebly for a few seconds, and then remained still, and seemed wholly to have lost its power. In about half a minute it again began to beat, and in a few minutes acquired considerable power, and again supported the circulation. It beat more feebly, however, than before the spinal marrow was destroyed. It ceased to beat in about an hour and a half after the brain had been destroyed. In another frog, after the brain and spinal marrow had been wholly removed without any further injury being done to them, the heart beat for nine hours, gradually becoming more languid.

JAMES BLACK

James Black (1788-1867), a Scottish physician who had studied at Glasgow and Edinburgh, conducted a series of experiments of extraordinary interest upon the reactions of the capillaries and published his results in a book the title-page of which is given in Fig. 19. Black considered the question of peripheral hearts, *i.e.* waves of peristalsis passing along the capillary vessels, as of possible assistance in the maintenance of the circulation in its terminal ramifications. He points out, however, that the constriction of a capillary vessel necessary for such peristalsis would in reality serve to impede rather than to assist the work of the heart. As the following paragraph will show,[22] Black observed contractility of the minute vessels in the webs of frogs' and ducks' feet. It is true that he did not prove the existence of independent contractility of the capillaries in the sense in which we now understand it, but he observed changes in their calibre which is of great significance in the light of recent work. The conclusions which he draws are noteworthy since they were put forward in the face of the dogma of Haller which continued to hold sway almost unchallenged until 1917-18. Black's studies might have received wider recognition had it not been for the fact that Marshall Hall a few years later published a book in which he denied the existence of capillary contractility.[23] Hall, however, was the first clearly to distinguish capillaries from arterioles on anatomical grounds.

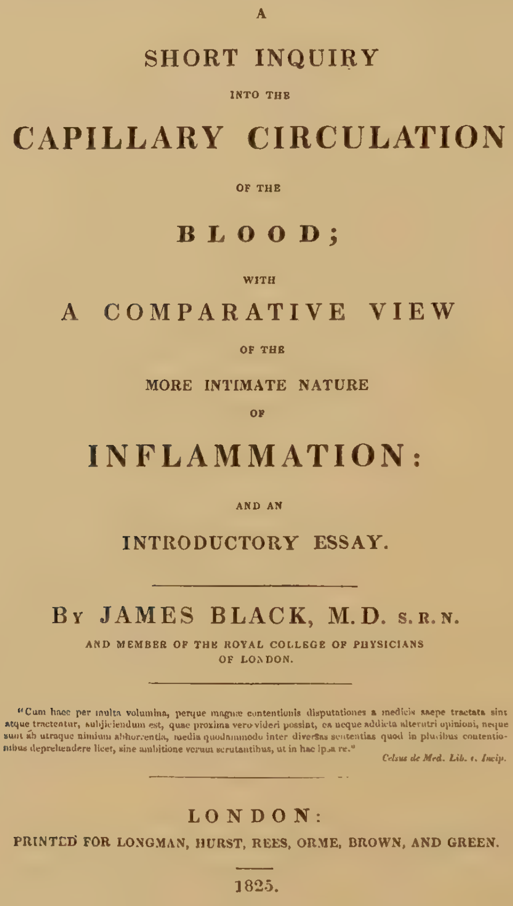
"*Exp. 4. On a frog.*—The natural circulation of the arteries in the web almost invisible, and without any red colour; but as soon as it was discovered, it was observed to circulate with considerable velocity, and the globules were not easily to be traced. Extension and gentle fastening of the foot even by the fingers, increased the flow of blood, and soon filled many of the colourless vessels with red globules. The application of Aq. Ammon., and more particularly of the salt solution, soon rendered the whole capillaries visible, and of double their former diameters; the circulation becoming slower, and congestion following in the veins, and lastly in the arteries.—The brain was crushed, and the circulation observed in the foot previously unexperimented upon. The vessels sooner than before became more visible, the circulation also became retarded, and congestion took place in the order of vessels as before remarked; but the circulation continued 20 minutes after the injury of the brain, and lastly the blood slowly retired from the smaller vessels of all descriptions, and left the web pale and flaccid."

---

[22] Black, J. *A short inquiry into the capillary circulation of the blood.* London: printed for Longman, Hurst, Rees, Orme, Brown, and Green, viii+118 pp., 1825 (pp. 54-55). The present editor has described Black's observations at greater length: "James Black's description of the independent contractility of capillaries." *The Lancet,* vol. 217, no. 5541, p. 1010, Nov. 9, 1929.

[23] Hall, M. *A critical and experimental essay on the circulation of the blood; especially as observed in the minute and capillary vessels of the batrachia and of fishes.* London: R. B. Seeley and W. Burnside, xviii+187 pp., 10 plates, 1831.

"*Exp. 5. The web of a young duck's foot was made the subject of this experiment.*—The veins in beautiful branches were easily seen by a common magnifying glass, but the arteries were only visible after some stimulation. The web could not be rendered transparent enough to see the red globules by the microscope. Aq. Ammon. was applied to both sides of one of the divisions of the foot; in two to four minutes great contraction took place in the large vessels; so much so, that many



A
SHORT INQUIRY
INTO THE
CAPILLARY CIRCULATION
OF THE
BLOOD;
WITH
A COMPARATIVE VIEW
OF THE
MORE INTIMATE NATURE
OF
INFLAMMATION:
AND AN
INTRODUCTORY ESSAY.

By JAMES BLACK, M.D. S.R.N.
AND MEMBER OF THE ROYAL COLLEGE OF PHYSICIANS
OF LONDON.

"Cum haec per multa volumina, perque magnae contentionis disputationes a medicis saepe tractata sint atque tractentur, subjiciendum est, quae proxima vero videri possint, ea neque addicta alterutri opinioni, neque sunt ab utraque nimium abhorrentia, media quodammodo inter diversas sententias quod in pluribus contentionibus deprehendere licet, sine ambitione verum scrutantibus, ut in hac ipsa re."
Celsus de Med. Lib. 1. Incip.

LONDON:
PRINTED FOR LONGMAN, HURST, REES, ORME, BROWN, AND GREEN.
1825.

FIGURE 19. The title-page of James Black's *Short inquiry into the capillary circulation of the blood,* 1825.

branches were rendered invisible, and others appeared like the finest hairs, which, before in their natural state, seemed three times the diameter. It was not a mere recession of the blood, for the line of the larger vessels was very distinctly contracted and well defined. After the space of about four minutes, all the vessels acquired their former natural diameters, and still further enlarged to complete phlogosis of the part, or to what may be termed inflammation. A fresh application of Aq. Ammon. produced a fresh contraction, but it was not near so complete as the former. The other foot was treated with a saturated solution of Mur. Sodæ, which application was soon followed by great enlargement of the vessels, especially of the larger veins in the web, which seemed much congested, until bathed on both sides with Aq. Ammon. when after five minutes, general contraction was produced, and many of the small vessels were rendered invisible.—During the above experiment, the animal scarcely struggled."

[On the basis of these and other observations Black draws 12 carefully worded conclusions, several of which may be given]

"*Third.*—The healthy and natural circulation in the capillaries depends, directly, on a tonic or *tensive* state of their delicate tubes; and mediately, on some power inherent in the part, a degree of which power seems to reside in the blood equally with the vessels, and its energy depends more on the integrity or vitality of the part or parts of this system, than upon any impulse derived from the heart."

"*Fifth.*—A strong stimulus suddenly applied, in a short time, produces a contraction of all the fibres of the part, and a diminution of the diameters of the whole classes of vessels, but more particularly of the arteries, which is followed, at a greater or less distance of time, by a corresponding dilatation—according to the extent of which, the phenomena of inflammation will be more or less observable; and more so, if the *vis a tergo* be powerful or stimulated."

"*Sixth.*—A gentle or lesser stimulus produces an evanescent contraction, followed by relaxation, increased redness, and a slight acceleration of blood in the *leading* capillary arteries and veins; owing, it seems, to the increased capacity of the distended reticular vessels, while the former are yet relatively contracted."

"*Seventh.*—The circulation in the capillary system is independent of the controul [sic] of the heart, except so far as this organ affords a constant pressure and a ready supply of blood, upon which the capillary vessels may act; and it is still more independent of the brain."

"*Tenth.*—The condition of a part, in what is termed inflammation, is essentially seated in the capillary vessels, and primarily and chiefly in those of the veins."

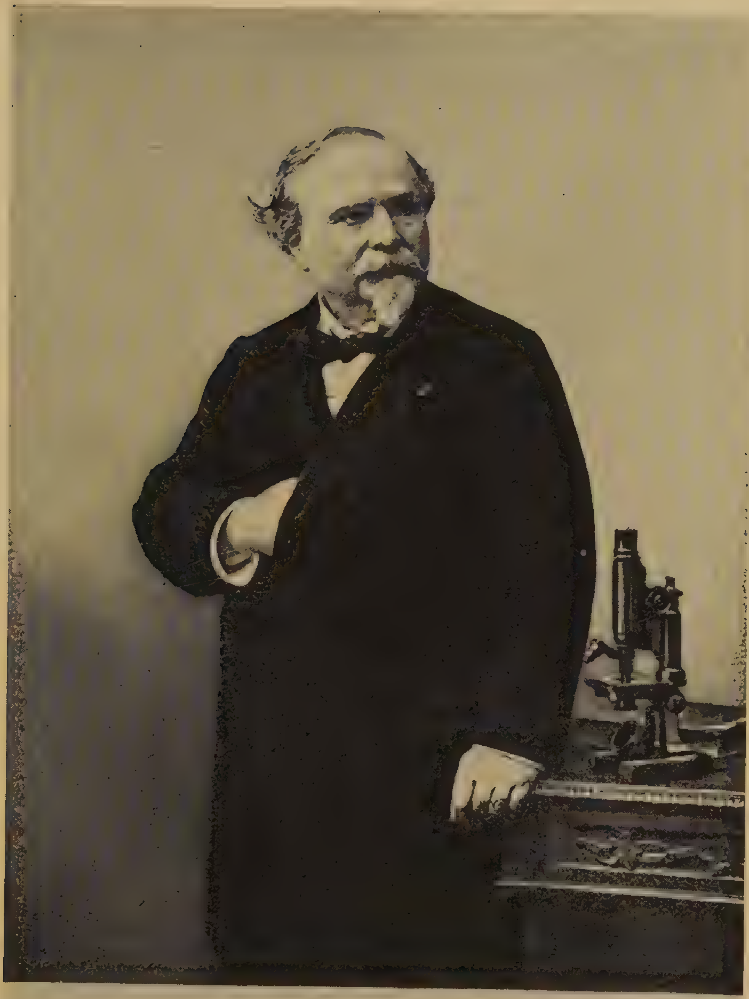
CHARLES-MARIE-BENJAMIN ROUGET

CHARLES-MARIE-BENJAMIN ROUGET (1824-1904), the son of a distinguished military surgeon of the army of the first Empire, was born at Gisors, and obtained his education at the Collège Sainte Barbé. He studied medicine at Paris and became an interne at the Hôtel Dieu, after which he accepted in 1860 the Chair of Physiology at the faculty of medicine at Montpellier. Following the death of Claude Bernard in 1878, a new Chair of General Physiology was created for Rouget at the Museum of Natural History in Paris; he came to occupy this post in 1879 and continued to hold it until 1893.[24] Rouget was a man of great energy and enthusiasm; he had a powerful yet kindly face and a military bearing, as is evident in the excellent engraving of him reproduced in Figure 20. He was an outstanding success as a teacher, lecturing always to crowded benches, and he counted among his pupils Mathias Duval and many well-known French clinicians. He was also an ardent histologist, and in 1867 *(Comptes rendus)* he propounded a theory of muscular contraction based upon the belief that the contractile elements in a muscle are arranged between the successive planes of a close helicoide—a point of view recently revived by Tiegs. His observations upon the contractile cells of the capillaries, however, represent a much more important and original contribution, particularly significant in the light of recent work, and in view of the neglect into which they had fallen prior to the papers of Vimptrup and Krogh, we give in translation below the full text of the two papers.[25]

---

[24] The details of Rouget's life are little known, and the chief source of information concerning him appears to be in the obituary notice by his successor, Nestor Gréhant in the *Nouvelles Archives du Muséum d'histoire Naturelle de Paris* (1904, 4 série, tom 6, pp. iii-xii), the last seven pages of which give a list of his papers. I am indebted to Dr. L. Hahn, the librarian of the Faculté de Médecine, Paris, for directing my attention to this notice and to Professor Louis Lapicque of the Sorbonne for obtaining the photograph of the engraving reproduced in Figure 20. Professor Lapicque, who was also a pupil of Rouget, has put down recollections of his master and has given the history of the Chair which he occupied ("La Chaire de physiologie du Muséum." *Rev. Scient.*, Paris, tom. 50, pp. 769-779, 1912).

[25] Rouget, Ch.-M-B. "Mémoire sur le développement de la tunique contractile des vaisseaux." *Comp. rend. Acad. Sci., Paris,* 1873, tom. 79, pp. 559-562. "Sur la contractilité des capillaires sanguins." *Ibid.*, 1879, tom. 88, pp. 916-918.



Ch. Rouget

FIGURE 20. Charles Rouget (1824-1904) (from the *Nouvelles Archives du Muséum d'Histoire Naturelle,* Paris, 1904, vol. 6).

NOTE ON THE DEVELOPMENT OF THE CONTRACTILE WALLS OF BLOOD VESSELS

Further research into the development of blood vessels, conducted since the early spring on the larvae of amphibians, proves beyond doubt the contractility of cells with ramified protoplasmic elongations which I observed last year in the blood vessels of the hyaloid membrane of an adult frog.

Indeed, identical cells in larvae constitute a so-called "adventitial" wall in arterial, venous and true capillaries. This wall being merely a continuation of the muscular walls of the arteries and veins, it follows that the whole blood vascular system, from the heart to the capillaries inclusive, is surrounded by a contractile wall.

The blood vessels of the dorsal fin of amphibian larvae—which, according to a commonly accepted error which I shared myself till last year, have the complete structure of primitive capillaries, *i.e.* one membrane only of parietal (endothelial) cells—should be, according to my most recent observations, classed not only from a functional but also from a structural point of view, into arteries, veins and a network of capillary vessels.

On living vessels thus contracted, one can see refracting annular constrictions projecting at the edges of the vessels to which they give a crenated appearance. Their surface on cross section partially reproduces that of the fibre cells of the arteries, and here and there widely separated nuclei are visible. The ramifications of the arterioles which gradually become more widely separated and even the capillary arches nearest the free edge of the tail and those of the intermediate capillary network, present the same appearance, but with a gradual diminution in the diameter of the constrictions and an increasingly marked scarcity of nuclei. The refracting annular constrictions and the nuclei belong to cells with ramified protoplasmic elongations absolutely identical with those which I previously observed on the vessels of the hyaloid membrane in an adult frog. Under the successive action of alcoholized water and of iodine solution, an anhistious membraneous tube, constricted at regular intervals by twisted contractile cellular filaments, dilated by imbibition of the primitive vascular tube and retracted in the centre of the membraneous sheath, was also visible on the blood vessels of the dorsal fin. All the vessels of the dorsal fin in the final stages of development have this fundamental structure, but for this one difference, in the capillaries the nuclei are very scarce and very widely separated from each other, the contractile filaments are very fine, their division appearing merely as a point, in the venules the nuclei are farther apart than in arterioles of the same order, while the cellular ramifications are finer, more irregular and distant from each other. In addition, the contractility of the veins is much less obvious on account of the distension of their walls by the blood driven back from the arteries and capillaries.

The first contractile cells which make their appearance in a recently-formed blood vessel, do not proceed either from the primitive vascular cells (endothelial), from which they are separated by a membraneous cuticle, or from the cells of the surrounding connective tissue with which they have no connexion at any stage in their development. On the contrary I have often observed that in young vessels, as yet lacking a contractile tunic, the ameboid cells spread their elongations over their walls, as do later the ramified ameboid pigmentary cells, which are properly speaking the first constituent elements of the wall of connective or adventitial tissue. Comparing these observations with those which I made previously on the rôle of ameboid cells (leucocytes) in the formation of the secondary wall of the blood vessels of the hyaloid in the embryos of mammals, it follows that not only are the walls of connective tissue, the adventitial walls of the arteries, veins and neurilemma, made up of migratory cellular elements which attach themselves to the nerve vessels and cords, but also contractile tissue of a higher order may have the same origin.

THE CONTRACTILITY OF BLOOD CAPILLARIES [1879]

Five years ago I communicated to the Academy the first results of my observations on the contractility of the blood vessels of the dorsal fin of tadpoles. All these vessels are contractile and they do not owe this property to the endothelium—which, as I have shown, is entirely made up of cells of naked vacuolar protoplasm—but rather to a network of ramified contractile cells, whose existence I previously established for the first time in the capillaries of the hyaloid membrane of adult frogs.

If tadpoles are submitted to the action of an anaesthetic so as to produce the beginnings of syncope, one can see the distributing arteries which emerge from the caudal arterial trunk contract and shrink till the lumen of the vessel disappears at the numerous annular constrictions, especially near the point of branching. Local stimulation, whether mechanical, chemical or electrical, causes annular constrictions at the point excited; but, in addition, following similar stimulation of a cut surface of the tail on a living animal—*i.e.* on the nerve and vascular trunks from which the ramifications of the dorsal fin arise—the blood immediately flows back; this is entirely due to the contraction of the vessels themselves, chiefly that of the arterioles and their bifurcating branches in the capillary network; these, contracting slowly but strongly, cause a centripetal movement of the blood in all vessels; this movement may last 5 or 10 minutes after stimulation has ceased and drives all the blood from the capillaries into the veins. Even during contraction crenations are visible on the edge of the capillaries, which correspond to refracted annular strictures bearing here and there globular projecting nuclei, fairly far apart from each other. These constricting bands and nuclei are part of the contractile cells and their ramified protoplasmic elongations, the earliest embryonic form of the fusiform muscle cells of the vessels, developing from them in successive divisions.

Recent observations on the blood vessels of the nictitating membrane of mammals, either newly-born or in embryos of various ages, show that the same phenomenon of contractility observed in the larvae of batrachians is also present accompanied in the same way by a return of circulation in vessels isolated from the heart, whether provoked by mechanical stimulation or appearing at the onset of rigor. This contractility also belongs properly to the ramified protoplasmic cells which surround the endothelial wall in a network. I have found the same structure in the capillaries of the epiploon (omentum) of young mammals and in those of the electric organ of the eel.

Without contractility the capillaries would not be able to rid themselves of the blood which they contain. Even in animals bled to death I have found the capillaries swollen with blood immediately after death when they had not previously contracted in the death-agony and before rigor had set in. However complete may be the contraction of the small arteries it could not—as has been believed up till now—empty the capillaries of their contents; it could only act like a tap placed on the course of a tube through which a liquid flows. When the flow is interrupted, even if the tube were elastic, that part of it which is above the tap and therefore escapes its pressure, would not be emptied. Not only would a network of capillaries, which escapes pressure of the heart owing to the closing of the small arteries, not empty itself, but blood from the veins would flow into it; the absolutely bloodless condition of a living part, such as the skin of the face under the influence of emotion, or the extremities when exposed to long continued cold, can only be explained by actual contraction of the capillaries.

While studying, in 1874, the development of the capillaries of the nictitating membrane in the embryos of mammals, I described and depicted the adventitial wall of these vessels as made up of migratory cellular elements, which come and attach themselves to the outside of the endothelium—as occurs in the case of batrachian tadpoles. I have since realised that this adventitial wall is nothing more or less than the contractile wall itself. However strange this origin of muscular elements may seem, it has been recently confirmed (in 1878) by Professor Selenka of Erlangen, who has seen and described in embryos of holothuria tubulosa the muscular bed of the intestines, which is made up of migratory ameboid cells which come and attach themselves to the exterior of the intestinal mucosa. I consider, therefore, that I am justified in concluding that, in all vertebrates, a similar contractile tunic, modified only in the form of its elements, surrounds the whole system of the blood vascular channels, from the heart to the capillaries inclusive, and that its contractility—the character of whose manifestations is also modified according to its situation—is an essential property of every part of the vascular system.

AUGUST KROGH

Schack August Steenberg Krogh, the Professor of Zoö-physiology at the University of Copenhagen, was well known to physiologists prior to 1918 for his investigations on metabolism, the volume output of the heart, and respiration. In that year there began to appear a series of notable papers on the physiology of capillaries, which culminated in his Silliman Lectures at Yale in 1922. Krogh and Lewis together almost literally rediscovered the capillaries and have made this field peculiarly their own. Krogh's observations upon the shifting of open capillaries in resting tissue, which is described in the following paragraphs, may well be regarded as one of the great contributions to modern physiology.[26]

CAPILLARY BED DURING ACTIVITY

My own first contribution to the problem of capillary contractility was published in Danish in 1918, about a month after Dale and

---

[26] Krogh, S. A. S. *The anatomy and physiology of capillaries* (Silliman Memorial Lectures). New Haven: Yale University Press, xvii+276 pp., 1922 (pp. 37-39 and 172-174). Second edition 1929.

Richards' paper, and somewhat later appeared in the British *Journal of Physiology* (1919). It was undertaken to test the hypothesis of a regulation of the supply of blood to muscles through the opening and closing of individual capillaries. I found it possible to observe at least the superficial capillaries of muscles both in the frog and in mammals through a binocular microscope, using strong reflected light as a source of illumination. Resting muscles observed in this way are usually quite pale, and the microscope reveals only a few capillaries at fairly regular intervals. These capillaries are so narrow that red corpuscles can pass through only at a slow rate and with a change of form from the ordinary flat discs to elongated sausages. When the muscle under observation is stimulated to contractions a large number of capillaries become visible and dilated, and the rate of circulation through them is greatly increased. When the stimulus has lasted only a few seconds the circulation returns in some minutes to the resting state; the capillaries become narrower and most of them are emptied completely, while a small number remain open. Since capillaries, even in a group fed by the same arteriole, do not all behave in the same way, the changes obviously cannot be due to arterial pressure changes.

In resting muscles of the frog the average distance between open capillaries, observed simultaneously through the microscope, was estimated at 200 to 800μ, but after contractions this could be reduced to 70 or 60μ. In the guinea pig average distances of about 200μ could be observed during rest. The exposure to the air and the strong light always increased the circulation, and it was often possible to see the circulation begin in one capillary after another.

It might be argued that the observations here recorded could be explained as the results of dilatation of arterioles alone, on the assumption that the capillary paths offer various degrees of resistance, that a few are opened by a low pressure, while the majority of capillaries belonging to an arteriole require a higher pressure and are opened only when that arteriole is dilated. Such an assumption would involve as a consequence that a reduction of the pressure to 0 by cutting the artery must produce an elastic contraction and emptying of the postulated high-pressure capillaries. Numerous observations have shown that all the capillaries may remain open when a piece of muscle is cut out after stimulation.

THE SHIFTING OF OPEN CAPILLARIES IN THE SKIN AND OTHER TISSUES

On the back of the hand it is usually possible to see only the tips of the capillaries, but occasionally the venous branch may be traced all the way to the richly anastomosing network of venules below, and we can see this horizontal plexus receive the blood from the capillary loops at regular intervals.

When a single small field is watched over a period of several minutes, it is found that here, unlike the conditions at the base of the nail, all the capillaries are not open at a given moment. They are opening and closing continuously, as seen in the figure, where drawings made every three minutes have been reproduced, together with a representation of all the capillaries present in this field, and opened up by the stimulus of a light pressure. Similar shifting of the open capillaries over the field has been observed again and again in the human skin when in a completely unstimulated condition. Hagen has seen corresponding changes in a flat capillary network in the rabbit's ear and given a diagrammatic representation of a number of changes taking place during a few minutes. They also regularly occur, though they are not so conspicuous, in the web of frogs, as I have described (1921), and I have seen them repeatedly in frogs' muscles. Quite recently a shifting of the blood flow from one capillary to another and from one glomerulus to another has been described by Richards (1922) for the frog's kidney.

I intend to apply cinematograph methods to make a closer and more extended study of these shiftings of open capillaries than is practicable by visual methods, because I believe them to represent the very essence of capillary circulation regulation.

A very small number of open capillaries (compared with the total number existing) is sufficient, as we have seen, to supply the wants of a resting tissue, but if the open capillaries were always the same the distribution of the substances supplied by them would be very unequal. The tissue elements nearest to the open capillaries would get more than they required, and the more distant would be starved. When the position of the open capillaries is continuously changing, a cell, starving at one moment, will get all it wants when the capillary nearest to it is opened up. In this way an adequate, though intermittent, supply can be secured at every single point, while, at the same time, the blood is utilized with the utmost economy, the necessary minimum only being present at any one time in any tissue.

A regulation of this kind may possibly be brought about by metabolic products accumulating at points where the distance through which they have to diffuse in order to reach an open capillary is too great, and by their action causing the opening of a nearer vessel. It may be conceived as simply due to oxygen lack—in some tissues at least— and it may be due, perhaps, to the pituitary hormone, which gradually disappears from a capillary when it is closed to the passage of blood. It is at present impossible to make a choice between these and other possibilities. Several factors may work together, and all I can say is that the problem requires and will undoubtedly repay the most careful experimental investigation.

In the skin of man and, very noticeably, in the palm of the hands, there is a further shifting of open capillaries (and venules), in so far as fields of a few millimeters diameter in which there are only a few open capillaries, while the underlying vessels are indistinct, alternate with others in which a large number of capillaries are open and the underlying vessels are prominent. The difference is often quite distinct when seen with the naked eye (Ebbecke, 1917, p. 51), and it can be observed how the white and red spots may be continually changing in form and location.

THOMAS LEWIS

Sir Thomas Lewis, cardiologist and authority on the circulation in the human skin, has done as much as any other individual of the present day to introduce scientific methods of thought and investigation into clinical medicine. His contribution to pure physiology has also been prodigious; in his work and teaching he has effectively bridged the chasm between the laboratory and clinic,—to the lasting benefit of both,—and he has taught an increasing and enthusiastic body of pupils how best to adapt the experimental method to the needs of clinical medicine. The influence which he is exerting can be judged by the rich fruition of his own labours and of those of his followers in various parts of the world. His simple and well-conceived experiments, his painstaking observations and carefully worded conclusions are nowhere, it seems to me, better illustrated than in the following passage from his recent monograph on the human capillaries.[27]

THE WHITE REACTION

Pallor of the skin can be produced, as will be seen, in one or other of several ways; but first we may consider the white reaction to a mechanical stimulus. If a blunt point is drawn with light pressure across the warm skin of the forearm or back, the skin pressed upon blanches as the point travels over it. This blanching results from a simple and temporary displacement of blood from the superficial vessels of the skin; the natural skin colour returns and the white track in the wake of the travelling point is obliterated almost as soon as it is formed. The skin over which the point has passed is now uniform in colour but, within a period varying usually from 15 to 20 seconds, the line of stroke again becomes visibly paler than its surroundings. After usually a half or a whole minute, this narrow band of pallor is of full intensity. . . . .

---

[27] Lewis, T. *The blood vessels of the human skin and their responses.* London: Shaw and Sons, xv+322 pp., 1927 (pp. 23, 25-29, 30).

Reduction in the size of the vessels that are responsible for skin colour has manifestly happened in the white reaction; and it might be natural to attribute this change to contraction of the arterioles supplying the corresponding area of skin; for such arteriolar constriction could be said to lower the distending pressure in the minute vessels and these would tend to become emptier as a consequence. But we were reluctant to accept such an explanation for the reason stated, namely, the sharpness with which the area stimulated is subsequently marked out by the reaction; there is the additional argument that obliteration of the brachial artery does not empty the minute vessels nor produce pallor of nearly the intensity that is seen in the white reaction. There remained the possibility that the reaction is due, not to a passive effect of arteriolar constriction, but to an active change in the minute vessels themselves.

The following experiment was devised finally to differentiate between the two last causes. An armlet is placed on the upper arm of a subject, the skin of whose forearm is known to yield a conspicuous white reaction to a stroke, and a pressure of 250 to 300 mm. Hg. is thrown abruptly into the armlet from a large pressure reservoir. The flow in the brachial artery and veins is instantly obstructed by this procedure and the onward flow in the capillaries of the lower arm rapidly ceases. Since, at the moment of compression, the pressure within the arteries is higher than in the veins, flow does not cease at once; but it does cease, as direct observation of the capillaries of the nail bed shows, within a very short time, namely within ½ to 1 minute (Neumann 1920, and personal observations). Kendrew (1926), working in my laboratory, found that the pressure in the veins rises for about these periods after the pressure is applied. The pressures in the vessels of the arm as a whole enter a state of general equilibrium and this state is subsequently maintained. If the two arms are now stroked simultaneously, the white reaction appears on both. Within observational error, it appears simultaneously on the two arms, is equally vivid on the two, and fades away in much the same time. Briefly, the reaction is not affected when the circulation in the limb is stopped. A white reaction may be obtained in the skin of such a limb when its main vessels have been firmly compressed for periods of 5, 10, or sometimes even 15 minutes. . . . .

The appearance of a white reaction to stroking, when the circulation has been brought to rest, is an event of prime importance, for it is incompatible with a belief that the reaction is due to stimulation of the arterioles. It proves that the walls of the minute vessels contract and expel their contents. When the circulation has been stopped, an arteriolar contraction, if it affects the minute vessels at all, can only increase their contents. The reaction occurs in the walls of those vessels that are responsible for skin colour, and not in the walls of vessels conveying blood to these. It is an active and not a passive effect in the vessels that are under examination. This observation, made 11 years ago,[28] and the conclusion then based on it that "we are forced to regard the tissue elements immediately surrounding the capillary blood and forming an essential layer of the capillary wall as the source of the reaction," is to be emphasised.

The reasons for placing these crucial observations in the foreground are several. The first will be apparent at once; the observations are undertaken upon the human subject and the conclusion applies to *human* capillaries and venules, thereby adding to its value. Secondly, the actual observations are of the simplest character, easy to repeat and demonstrate; for this reason and because the appearances are manifest they are the more convincing; likewise their interpretation is freed from many minor sources of error; for there is in this case minimal disturbance of the living structures concerned in what is evidently a delicate reaction. Thirdly, because they serve to illustrate the truth that a conclusion is suggested or may be reached from every distinct phenomenon observed, however simple or trivial such observations may at first sight seem, and that sometimes, as here, the conclusion may possess a far reaching application, if based on observations properly controlled. Fourthly, because the conclusion has proved unassailable; it formed the first of those demonstrations that during the last decade have converted physiologists to their recent and now almost universal belief in the important part played by the capillaries in controlling the circulation.

---

[28] That is, in 1917. Cotton, T. F., Slade, J. G. and Lewis, T. "Observations upon dermatographism with special reference to the contractile power of capillaries." *Heart,* 1915-17, vi, pp. 227-247.

CHAPTER IV

RESPIRATION

PRIMITIVE man must have been quick to recognize that respiratory movements, like the pulse, were essential to life, but the real significance of breathing had to await the discovery of the circulation of the blood. Galen and Aristotle had taught that the air which passed into the lungs served merely to cool the heart, for this organ, the seat of life, tended to be destroyed by the heat which it generated. The ancients, however, also taught that breathing facilitated the removal from the body of the "fuliginous vapours," by-products of burning of the body tissues, especially the heart. Fabricius (1615) in his little book on respiration re-echoed the Galenical doctrine. Vesalius (1543), however, had carried out artificial respiration on animals, observing that the heart beat became weak and the arteries pulseless after he ceased to work the bellows, reviving again when the ventilation was renewed. With the discovery of the circulation various speculations were entertained concerning the exchange of substances between blood and air. Some postulated the existence of pores connecting the air spaces with the blood. Malpighi established that the bronchi terminated in minute air spaces in close proximity to the capillary vessels which he also discovered. Boyle, in 1660, performed the fundamental experiment of showing that a partial vacuum extinguished life at the same time that it abolished the burning of a candle. Robert Hooke studied artificial respiration in dogs, proving that the lungs expanded by virtue of movements of the chest wall and that even this was unnecessary for life provided that adequate aeration were obtained by a constant flow of air through a uniformly expanded lung. Lower observed venous blood to become bright red on passing through the lungs and on being exposed to pure air. Mayow proved conclusively that a portion of the air, the spiritus nitro-aereus, sufficed for life; and he added with singular appropriateness that "nitre has made as much noise in philosophy as in war." Mayow also gave a detailed description of the mechanics of the respiratory movements. These were the important contributions in the early history of respiration and it remained only for Priestley and Lavoisier to discover oxygen and for Haldane and Priestley to define the activity of carbon-dioxide as a normal stimulus to the respiratory centre of the brain, a centre which Legallois and Flourens had established anatomically in the early 19th century. Recent developments have turned upon the analysis of chronic oxygen-lack—mountain-sickness—and on the related analysis of the dissociation curve of haemoglobin, to which Barcroft and his pupils have made notable contributions. Finally, tissue respiration has come to the fore, largely through the discovery of the first enzymic respiratory system, glutathione.

ROBERT BOYLE

ROBERT BOYLE (1627-1692), whose life and scientific contributions are described elsewhere, added notably to knowledge of respiration through study of the effect of states of low and high pressures upon the activity of animals. It is interesting that with the invention of the air-pump he was led almost at once to compare the burning of a candle with vital activities, noting that both ceased to occur in an exhausted vessel. Boyle began his observations as early as 1659 and continued them at odd times throughout a period of more than twenty years. The first passage is taken from the *Spring and Weight of the Air,* 1660,[1] and the second from the second part of *A Continuation of New Experiments Physico-Mechanical touching the Spring and Weight of the Air,* 1682.[2]

NECESSITY OF AIR FOR RESPIRATION AND COMBUSTION

Another Opinion there is touching Respiration, which makes the genuine use of it to be Ventilation (not of the Heart, but) of the Blood, in its passage thorow the Lungs; in which passage, it is disburthened of those Excrementitious Steams, proceeding, for the most part, from the superfluous Serosities of the Blood, (we may adde) and of the *Chyle* too, which (by those new Conduits of late very happily detected by the famous *Pecquet*) hath been newly mix'd with it in the Heart). And this Opinion is that of the Industrious *Moebius,* and is said to have been that of that excellent Philosopher *Gassendus;* and hath been in part an Opinion almost vulgar: But this *Hypothesis* may be explicated two ways: For first, The necessity of the Air in Respiration, may be suppos'd to proceed from hence; That as a Flame cannot long burn in a narrow and close place, because the Fuliginous Steams it uncessantly throws out, cannot be long receiv'd into the ambient Body; which after a while growing too full of them, to admit any more, stifles the flame, so that the vital Fire in the Heart requires an ambient Body, of a yielding nature, to receive into it the superfluous Serosities and other Recrements of the Blood, whose seasonable Expulsion is requisite to depurate the Mass of Blood, and make it fit both to Circulate, and to maintain the vital heat residing in the Heart. The other way of explicating the above-mentioned *Hypothesis,* is, by supposing, that the Air does not onely, as a Receptacle, admit into its Pores the Excrementitious vapors of the Blood, when they are expell'd through the Wind-Pipe, but does also convey them out of the Lungs, in regard that the inspired Air, reaching to all the ends of the *Aspera Arteria,* does there associate it self with the Exhalations of the circulating Blood, and when 'tis exploded, carrys them away with it self, as we see that winds speedily dry up the surfaces of wet Bodies, not to say any thing of what we formerly observ'd touching our Liquor, whose fumes were strangely elevated upon the Ingress of the Air.

---

[1] Boyle, R. *New Experiments Physico-Mechanicall, touching the Spring of the Air, and its Effects (Made, for the most part, in a New Pneumatical Engine).* Oxford: H. Hall, 14 leaves, 399 pp., 1660 (pp. 350-352).

[2] Boyle, R. *A Continuation of new Experiments Physico-Mechanical, touching the Spring and Weight of the Air, and their Effects. The Second Part . . . . .* London: Miles Flesher, 9+3 leaves, 198 pp., 1682 (p. 94).

Now of these two ways of explicating the use of Respiration, our Engine affords us this Objection against the first; That upon the Exsuction of the Air, the Animals die a great deal sooner then if it were left in the Vessel; though by that Exsuction the ambient space is left much more free to receive the steams that are either breathed out of the Lungs of the Animal, or discharg'd by insensible Transpiration through the Pores of his Skin.

EXPERIMENT XI

October 1, 1678

About 10 of the Clock in the morning, I included a Shrew-Mouse with common Air, in a Receiver, fortified against the external Air; about 11 the Mouse was brought to such straits, that he could hardly breathe: I threw in another strong and lusty Mouse into the same Receiver, and presently put on the stopple again: But because the first Mouse had consumed some of the Air, it came to pass that the external Air was forcibly impelled into the Receiver, and so was able to dispel a great part of the Air stagnant there; and indeed, when this was done, the first Mouse seemed to be much better, neither did it die much sooner than the other, but both of them died about noon. About 4 in the afternoon, I thrust a fresh strong Mouse into the same Receiver, and lest the external Air might again expel the included Air, I put him in very slowly and liesurely; The issue was, that this third Mouse lived not 3 minutes entire.

Whence we may conjecture, That that portion of Air which hath once served the respiration of Animals as much as it could, is no longer useful for the respiration of another Animal, at least of the same kind.

ROBERT HOOKE

Robert Hooke (1635-1703) started his career as a chorister at Christ Church, Oxford, later becoming Robert Boyle's technical assistant; as such Hooke designed and probably built with his own hand the first air-pump, thus making possible the great experiments on the 'Spring and Weight of the Air' which Boyle published in 1660 and 1662. Hooke's genius soon became evident and Boyle was quick to recognize it and to give him full credit. He was one of the early Fellows of the Royal Society (1663), becoming their Curator, and he frequently carried out experiments at their meetings. On October 24th, 1667, he demonstrated how animals may be kept alive by blowing air through their lungs with bellows, and the published account of this experiment contained one of the more important advances in the history of respiration, for Hooke had proved that respiration depended, not upon the movements of the lungs, but upon the flow of pure air through them.[3] In his book *Micrographia* (London, 1667) he also published remarkable observations on combustion which are available in the *Alembic Club* reprint (No. 5, 1902).

An Account of an Experiment made by M. Hook, of Preserving Animals alive by Blowing through their Lungs with Bellows

This Noble Experiment came not to the Publisher's *hands, till all the preceding Particulars were already sent to Press, and almost all Printed off, (for which cause also it could not be mentioned among the* Contents:) *And it might have been reserved for the next opportunity, had not the considerableness thereof been a motive to hasten its Publication. It shall be here annexed in the Ingenious* Author *his own words, as he presented it to the* Royal Society, Octob. 24. 1667. *The Experiment it*

---

[3] Hooke, R. "An account of an experiment made by M. Hook, of preserving animals alive by blowing through their lungs with bellows." *Phil. Trans. Roy. Soc.*, vol. 2, pp. 539-540, 1667. The collected works of Robert Hooke have been issued by the Oxford Press, under the editorship of R. T. Gunther as volumes 6 and 7 of *Early Science in Oxford* (1930).

self having been both *repeated (after a former successful trial of it, made by the same hand a good while agoe)* and *improved the week before, at their* publick Assembly. *The Relation it self followes:*

I Did heretofore give this *Illustrious Society* an account of an Experiment I formerly tryed of keeping a Dog alive after his *Thorax* was all display'd by the cutting away of the Ribbs and *Diaphragme*; and after the *Pericardium* of the Heart was also taken off. But divers persons seeming to doubt of the certainty of the Experiment (by reason that some Tryals made of this matter by some other hands, failed of success) I caus'd at the last Meeting the same Experiment to be shewn in the presence of this *Noble Company,* and that with the same success, as it had been made by me at first; the Dog being kept alive by the Reciprocal blowing up of his Lungs with Bellowes, and they suffered to subside, for the space of an Hour or more, after his *Thorax* had been so display'd, and his *Aspera arteria* cut off just below the *Epiglottis,* and bound upon the nose of the Bellows.

And because some Eminent Physitians had affirm'd, that the *Motion of the Lungs* was necessary to Life upon the account of promoting the Circulation of the Blood, and that it was conceiv'd the Animal would immediately be suffocated as soon as the Lungs should cease to be moved, I did (the better to fortifie my own *Hypothesis* of this Matter, and to be the better able to judge of several others) make the following additional Experiment; *viz.*

The Dog having been kept alive, (as I have now mentioned) for above an houre, in which time the Tryal had been often repeated, in suffering the Dog to fall into *Convulsive* motions by ceasing to blow the Bellows, and permitting the Lungs to subside and lye still, and of suddenly reviving him again by renewing the blast, and consequently the motion of the Lungs: This, I say, having been done, and the Judicious Spectators fully satisfied of the reallity of the former Experiment; I caused another pair of Bellowes to be immediately join'd to the first, by a contrivance, I had prepar'd, and pricking all the outer coat of the Lungs with the slender point of a very sharp pen-knife, this second pair of Bellows was mov'd very quick, whereby the first pair was alwayes kept full and alwayes blowing into the Lungs; by which the Lungs were also alwayes kept very full, and without any motion; there being a continued Blast of Air forc'd into the Lungs by the first pair of Bellows, supplying it as fast, as it could find its way quite through the Coat of the Lungs, by the small holes pricked in it, as was said before. This being continued for a pretty while, the Dog, as I expected, lay still, as before, his Eyes being all the time very quick, and his Heart beating very regularly: But, upon ceasing this blast, and suffering the Lungs to fall and lye still, the Dogg would immediately fall into Dying convulsive fits; but be as soon reviv'd again by the renewing the fulness of his Lungs, with the constant blast of fresh Air.

Towards the latter end of this Experiment a piece of the Lungs was cut quite off; where 'twas observable, that the Blood did freely circulate, and pass thorow the Lungs, not only when the Lungs were kept thus constantly extended, but also when they were suffer'd to subside and lye still. Which seem to be Arguments, that as the *bare* Motion of the Lungs *without fresh Air* contributes nothing to the life of the Animal, he being found to survive as well when they were not mov'd as when they were; so it was not the subsiding or movelesness of the Lungs, that was the immediate cause of Death, or the stopping the Circulation of the Blood through the Lungs, but the *want* of a sufficient *supply of fresh Air.*

I shall shortly further try, whether the suffering the Blood to circulate through a vessel, so as it may be openly exposed to the fresh Air, will not suffice for the life of an Animal; and make some other Experiments, which, I hope, will thoroughly discover the *Genuine use of Respiration*; and afterwards consider of what benefit this may be to Mankinde.

JOHN MAYOW

John Mayow (1645-1679), another of that constellation of Oxford physiologists which included Lower, Willis, Boyle, and Hooke among its number, is perhaps best known for defining as a definite chemical entity the substance we now know to have been oxygen, termed by him 'spiritus nitro-aereus.' Mayow was a shy man to whom personal slights loomed large, and the failure of his contemporaries to appreciate the significance of his work may be accredited as a factor in causing his untimely and unhappy death. There is a curious incident relating to the publication of his first scientific work, the so-called *Tractatus duo,* the title page of which is reproduced in fig. 21A. This work included an account of his memorable experiments on respiration, from which quotation is made below,[4] and his tract on rickets. It appeared, as is evident from a review published in the *Philosophical Transactions,* in November, 1668, and there is one copy still in existence in the Royal College of Surgeons which bears an original title-page with the date 1668. All others known to exist bear a cancelled title-page with the date 1669 (Fig. 21A). It seems that the seventeenth century printer, wishing to have his books appear up to date, destroyed at the end of the year title-pages of unsold copies, and substituted new titles with the new year. Oldenburg's review in the *Philosophical Transactions* was patronizing and unfortunate, and the sensitive Mayow probably never recovered from being so damned by faint praise. Shortly before his death he published at Oxford (from the Sheldonian Theatre, 1674) the two tracts included in the *Tractatus duo* with three others under the title *Tractatus quinque medico-physici. Quorum primus agit de sal-nitro, et spiritu nitro æreo.* In this, his last published work, is found the important tract on muscular movement. The full significance of Mayow's studies was not recognized until after Lavoisier had announced the discovery of oxygen. Thomas Beddoes, an erratic genius who fancied that with oxygen he could cure many of the ailments to which the flesh is heir, published an anonymous account of Mayow's work under the title *Chemical experiments and opinions extracted from a work published in the last century,* Oxford, 1790.

---

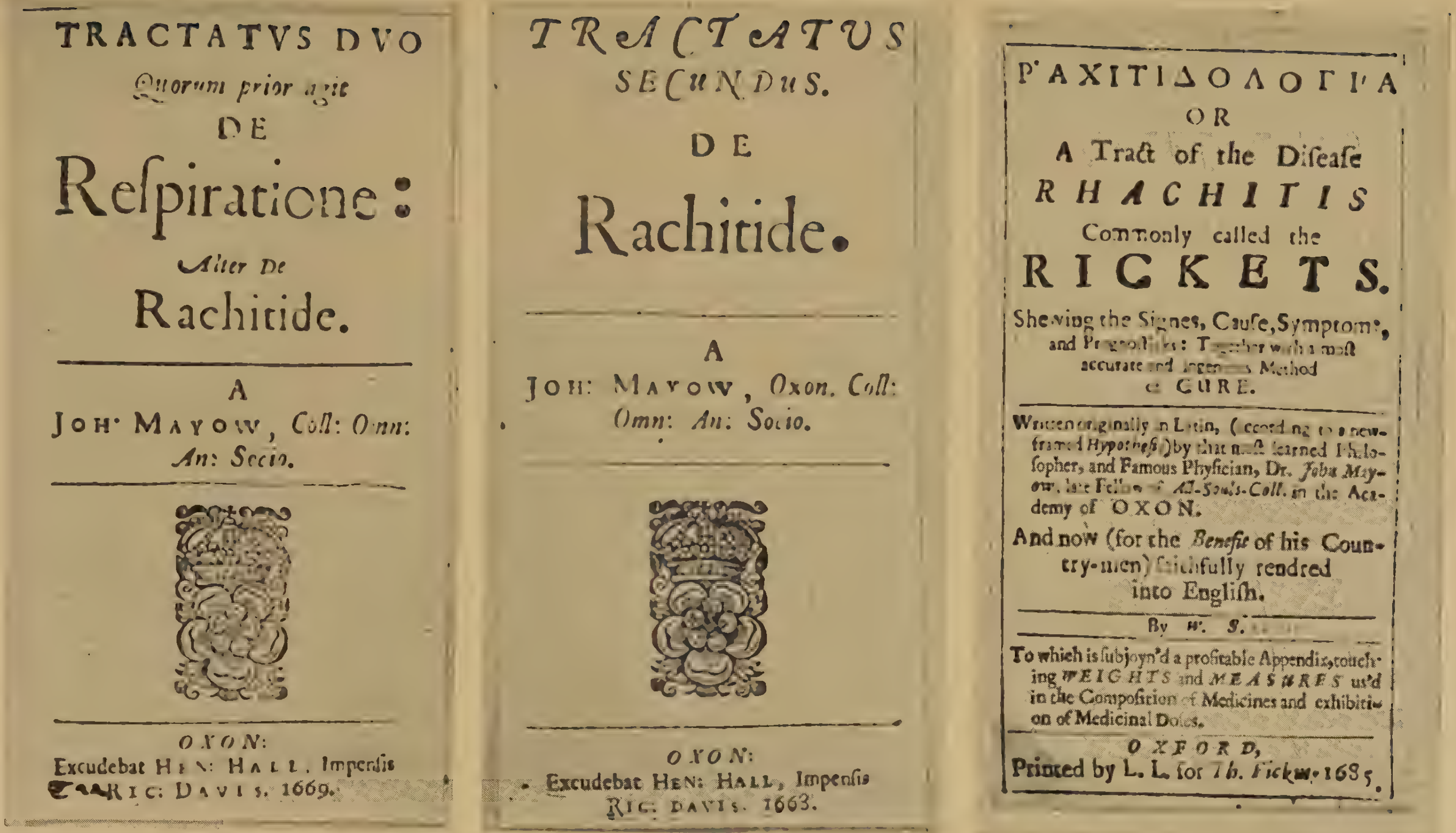
[4] Mayow, J. *Tractatus duo quorum prior agit de respiratione: alter de rachitide.* Oxford: Hen: Hall, Ric: Davis, 108 pp., 1668.

ON RESPIRATION

The lungs are placed in a recess so sacred and hidden that nature would seem to have specially withdrawn this part both from the eyes and from the intellect; for, beyond the wish, it has not as yet been granted to any one to fit a window to the breast and redeem from darkness the profounder secrets of nature. For of all the parts of the body, the lungs alone, as if shrinking from observation, cease from their movement and collapse at once on the first entrance of light and self-revelation. Hence such an ignorance of Respiration and a sort of holy wonder. Still, let me draw near to the inmost vitals, and, concerning so obscure a matter, make at least a guess.

In discussing on Respiration I shall follow the method pointed out by nature and begin therefore with inspiration. . . . .

With respect, then, to the entrance of the air into the lungs, I think it is to be maintained that it is caused in the following manner by the pressure of the atmosphere. For as the air, on account of the weight of the superincumbent atmosphere, not only rushes into all empty places, but also presses forcibly upon whatever is next it (as Boyle's experiments have put beyond doubt), it follows that the air, passed through the nostrils and the trachea, up to the bronchia or gates of the lungs, presses against the lungs from within and seeks an entrance into them. Hence it is that when the inner sides of the thorax (which by compressing the lungs from without were resisting the pressure of this air) are drawn



TRACTATVS DVO
Quorum prior agit
DE
Reſpiratione:
Alter De
Rachitide.

A
JOH: MAYOW, *Coll: Omn: An: Socio.*

OXON:
Excudebat HEN: HALL, Impenſis
RIC: DAVIS, 1669.

TRACTATUS
SECUNDUS.
DE
Rachitide.

A
JOH: MAYOW, *Oxon. Coll: Omn: An: Socio.*

OXON:
Excudebat HEN: HALL, Impenſis
RIC: DAVIS. 1668.

ῬΑΧΙΤΙΔΟΛΟΓΙΑ
OR
A Tract of the Diſeaſe
RHACHITIS
Commonly called the
RICKETS.
Shewing the Signes, Cauſe, Symptoms,
and Prognoſticks: Together with a moſt
accurate and ingenious Method
of CURE.

Written originally in Latin, (according to a new-framed *Hypotheſis*) by that moſt learned Philoſopher, and Famous Phyſician, Dr. *John Mayow*, late Fellow of *All-Souls-Coll.* in the Academy of OXON.

And now (for the *Benefit* of his Country-men) faithfully rendred into Engliſh.

By *W. S.*

To which is ſubjoyn'd a profitable Appendix, touching *WEIGHTS* and *MEASURES* us'd in the Compoſition of Medicines and exhibition of Medicinal Doſes.

OXFORD,
Printed by L. L. for *Th. Fickus*, 1685.

A B C

FIGURE 21. A. The cancelled title-page of Mayow's *Tractatus Duo* with the date of 1669 (original title 1668). B. The separate title of the tract on rickets with the date 1668. C. The first English translation of the tract on rickets.

outwards by muscles whose function it is to dilate the chest, and the space in the thorax is enlarged, the air which is nearest the bronchial inlets, now that every obstacle is removed, rushes under the full pressure of the atmosphere into the cavities of the lungs, and by inflating them occupies and fills the space of the expanded chest.

The structure of the lungs is adapted for their inflation as thus described, for their substance is composed, as the eminent Dr. Malpighi has noted, of very fine membranes, which form an almost infinite number of spherical vesicles whose mutual connection is such that there is easy access from the trachea to those nearest to it, and from these again to others. Consequently when these vesicles are inflated by an inrush of air, the whole substance of the lungs must necessarily expand. . . . .

Whenever, I say, a muscle attached to two bones contracts, the bone which is less fixed moves towards the other which is more fixed. Wherefore, since every lower rib is less fixed that the one above it, each of the lower ribs must be elevated when the intercostal muscles, even the internal ones, contract. For a quite similar reason holds with the internal as with the external muscles; nor is it an objection to this that the former are attached to the ribs in a different position, as is obvious from Plate I. [Fig. 22], where the interior muscle, a, a, will raise the lower and more mobile rib, in contracting, as well as the exterior muscle, b, b. And here it is to be noted that the ribs are so articulated with the spine that when they are pulled by the said muscles they easily ascend and are raised with rotation.

Nay, the very position of the muscles makes this plain, for if the interior muscle which is placed between the two lowest ribs were to pull the upper of the two downwards, all the ribs, since they are firmly attached to each other, would necessarily be drawn downwards at the same time, a thing which that weak and membrane-like muscle cannot do. How much more probable is it that the lower ribs are all drawn upwards together by the internal muscles between the upper ribs, for these are sufficiently strong and broad, while the weaker muscles between the lower ribs contribute merely to elevate the lower ribs. These things will be more clearly seen from Plate I [Fig. 22], which shows the ribs and the internal muscles.

And this view is also supported by the oblique and contrary position of the intercostal muscles. For Nature seems to have inserted these muscles obliquely in the ribs (although a direct insertion would have suited better for moving them up or down) because the intervals between the ribs are so small that if these muscles had been inserted at right angles, they would have been shorter than the nature of muscles admits. Wherefore, that these muscles should have a suitable length, they had to be inserted obliquely (as they are) to the ribs. Yet as this oblique position is less suitable for elevating the ribs, Nature, that most wise engineer, has arranged the muscles with divers aspects so that while they pull the ribs obliquely with equal force in this direction and in that, the ribs meanwhile rise straight upwards, as is shown in Plate II [Fig. 22], where, when the external muscle a, a, and the internal c, c, contract together, the lower and more mobile rib will rise not obliquely but straight upwards, just as though it were pulled by a muscle attached to

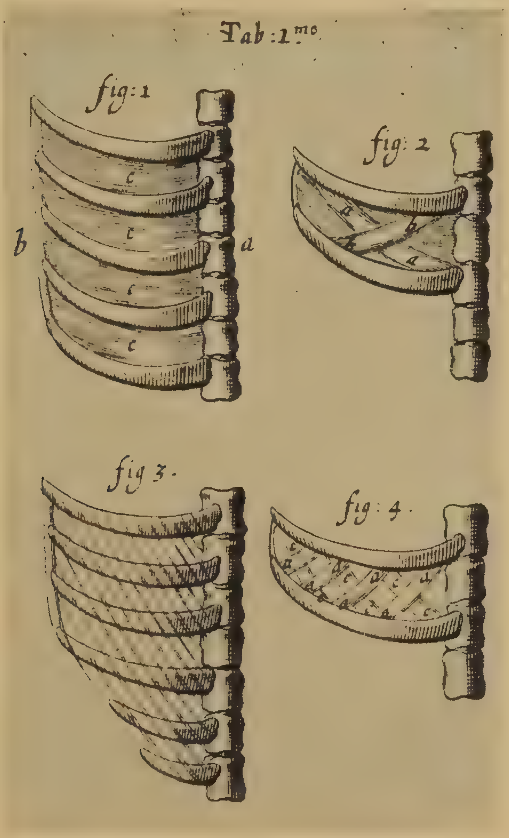


FIGURE 22. Mayow's figure, 1668, from his tract on respiration showing the action of the intercostal muscles.

it at right angles. So that clearly the external and internal muscles contract simultaneously, and by their united effort elevate the ribs and expand the chest. Moreover, that the internal muscles do not cause expiration, may be gathered from the fact that the thorax in a dead animal is always contracted, for to die and to expire mean the same thing; but in the dead, the action of the muscles altogether ceases; and so this contraction of the chest cannot be caused by the internal muscles, since they no longer contract. Should any one remark here that that contraction of the thorax is caused by the internal muscles immediately before the death of the animal, I ask, in reply, how then is it that the external muscles (since the two cases are similar) never contract in the dying, so that the chest should remain for some time dilated? . . . .

Similarly in *Orthopnœa,* in which the patient can only breathe in an erect position, it is probable that the abdominal viscera press too much on the diaphragm and keep it up in the chest, so that space enough for breathing cannot be provided in the thorax. If, however, the patient be placed in an upright position, the diaphragm, feeble though it be, aided by the weight of the same viscera, can force them downwards. And so, as the abdomen sinks, the chest dilates and the patient is able to breathe.

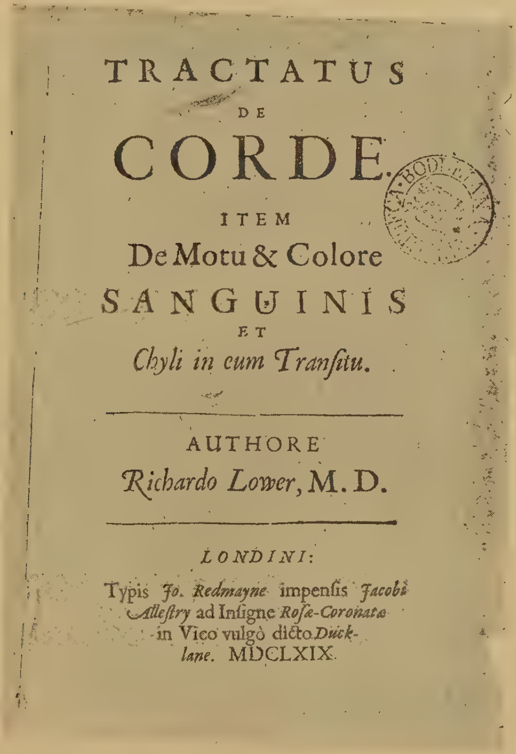
RICHARD LOWER

Richard Lower (1631-1691), a native of St. Tudy near Bodmin in Cornwall, where his family had lived for many generations, was also one of the group of Oxford physiologists which, shortly after the Restoration, laid the foundation of that preëminence which is still maintained by British physiologists. In February 1665 he carried out the first direct transfusion of blood from one animal to another and suggested that the manoeuvre might have a clinical application. An account of his experiments was published in the *Philosophical Transactions* in 1666 (vol. 3, pp. 226-232). Denys of Paris, adopting Lower's suggestion, carried out a transfusion upon a human being on June 15th, 1667. Those who are interested in blood transfusion should consult a remarkable two volume work by Scheel which deals exclusively with the history of the subject.[5] Lower's chief contribution to physiology was his book *De corde* (Fig. 23), published in London in 1669. He proved that the dark venous blood, when passed through the lungs became bright in colour and he suggested, as the following passage shows, that the blood absorbed from the air a definite chemical substance necessary for life, and that this was, in fact, the chief function of the pulmonary circulation.

[5] Scheel, P. *Die Transfusion des Blutes und Einsprützung der Arzeneyen in die Adern. Historisch und in Rücksicht auf die practische Heilkunde bearbeitet.* Copenhagen: F. Brummer. 2 Bd., xxiv+250 pp.; xvi+288 pp., 1802, 1803.

THE LUNGS AND THE COLOUR OF THE BLOOD

When I said previously that blood taken from a pulmonary vein is similar to venous blood, I was speaking from my own experience, and when I said that I was not then satisfied from my experiments that an animal can be kept alive if its lungs are full of air, the truth is that before I could reach the pulmonary vein and open it, all the air had passed from the lung. This last experiment, in which the animal is kept alive through its lungs being in a continual state of dilatation, was made by Mr. Hook and I learned how to do it from him.



TRACTATUS
DE
CORDE.
ITEM
De Motu & Colore
SANGUINIS
ET
Chyli in eum Tranſitu.

AUTHORE
Richardo Lower, M.D.

LONDINI:
Typis *Jo. Redmayne* impenſis *Jacobi*
Alleſtry ad Inſigne *Roſæ-Coronatæ*
in Vico vulgò dicto *Duck-*
lane. MDCLXIX.

FIGURE 23. The title-page of Lower's book on the heart, 1669.

If anyone should maintain that the red colour of blood ought to be attributed rather to the friction and separation of its corpuscles in the lung than to the mingling of the air with it, let him first consider whether the corpuscles of the blood undergo more friction and separation in the lungs than in all the muscles of the body (if it is possible that they undergo as much) and of a truth, since the lungs must be kept in a continual state of dilatation for this experiment, I do not see how the corpuscles can be separated except as they pass through the pores, in the same way as they do in passing through the whole system.

In addition, it is evident that this red colour is entirely due to the particles of the air which enter the blood, since it only becomes red in the lungs because of the direct and intimate intermingling which takes place between its corpuscles with the particles of the air, in the same way the surface of venous blood which is put onto a plate only takes on a red colour because it is exposed to the air, this is further proved by the certainty that if this surface were skimmed with a knife that which is immediately underneath would be changed in a short time to the same colour by a similar contact with the air.

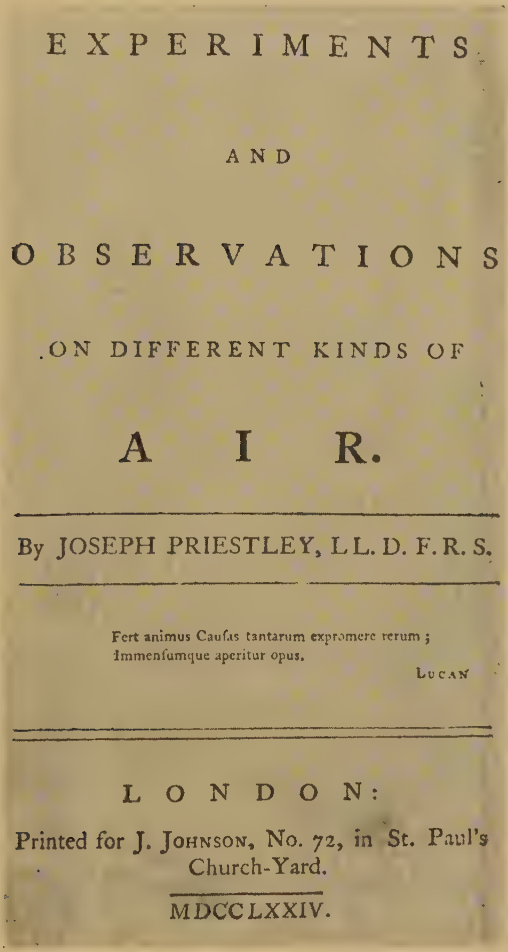
Moreover, if the thickest part of the blood is poured out after it has been standing for some time, its topmost surface soon becomes red, if the blood has not started to corrupt. Everyone knows that venous blood which has been put in a dish and stirred about for a long time so that the air passes through it, becomes red throughout, and I see no reason to be surprised that the separation and admixture of the air should cause such a change of colour in the blood, since other liquids also take on different colours according to whether their pores receive or reflect the rays of light in a greater or lesser degree.

If you ask me by which pores and passages of the lungs the essence of saltpetre in the air passes into the blood to fill it most abundantly, tell me, I pray you, by what pores and passages that other essence of saltpetre, contained in snow, passes through the cups and glasses of those epicures whose wines it cools in the heat of summer? If this spirit can penetrate glass and metal, how much more easily can it enter the lax and delicate vessels of the lungs. Finally, if we are agreed that sooty exhalations and watery humours find a passage, there is nothing to prevent us from believing that this nourishing saltpetre can enter the blood by the same or similar pores.

It is very probable, therefore, that the blood imbibes the air as it passes through the lungs and that its red colour is entirely due to this admixture, but after the greater part of the air has passed out of the blood as it goes through the whole system, through the parenchymae of the blood-vessels and is exhaled through the pores of the body; it is equally likely that venous blood, which lacks this essence, should be darker and blacker in appearance.

JOSEPH PRIESTLEY

Joseph Priestley (1733-1804) was born at Fieldhead, a farmhouse in Birstall parish, Yorkshire, and was educated at Daventry Academy. He served as parson at Needham Market in Suffolk, and later as Unitarian minister to a meeting-house in Cheshire. While there, he came in contact with that vigorous community in Warrington which, with John Aikin, Ferriar, Henry, and Percival, formed one of the most active centres of intellectual life in 18th century England. The Warrington Academy, to which Priestley was appointed in 1761, fed the



EXPERIMENTS

AND

OBSERVATIONS

ON DIFFERENT KINDS OF

AIR.

By JOSEPH PRIESTLEY, LL. D. F. R. S.

Fert animus Cauſas tantarum expromere rerum ;
Immenſumque aperitur opus.
Lucan

LONDON:

Printed for J. Johnson, No. 72, in St. Paul's
Church-Yard.

MDCCLXXIV.

Figure 24. The title-page of Priestley's *Experiments and observations upon different kinds of air,* 1774.

better known Manchester Philosophical Society with rich and varied intellects. Priestley's output during these years was prodigious. One finds his essays on education, a catechism for children, a long monograph on electricity, treatises on government, and later, numerous theological tracts. During the French Revolution his letter to Burke so enraged his fellow-townsmen that they burned his house and his manuscripts. He fled to America, where he lived till his death in 1804. Priestley's isolation of oxygen has been the subject of much dispute. That he prepared the pure gas is commonly accepted, but he could not divest himself of the doctrine of phlogiston, with the result that full credit for the discovery was left for Lavoisier. The following selections indicate the character of his observation.[6]

Section II

Of AIR *in which a* CANDLE, *or* BRIMSTONE, *has burned out*

It is well known that flame cannot subsist long without change of air, so that the common air is necessary to it, except in the case of substances, into the composition of which nitre enters; for these will burn *in vacuo,* in fixed air, and even under water, as is evident in some rockets, which are made for this purpose. The quantity of air which even a small flame requires to keep it burning is prodigious. It is generally said, that an ordinary candle *consumes,* as it is called, about a gallon in a minute. Considering this amazing consumption of air, by fires of all kinds, volcanoes, &c. it becomes a great object of philosophical inquiry, to ascertain what change is made in the constitution of the air by flame, and to discover what provision there is in nature for remedying the injury which the atmosphere receives by this means. . . . .

Though this experiment failed, I have been so happy, as by accident to have hit upon a method of restoring air, which has been injured by the burning of candles, and to have discovered at least one of the restoratives which nature employs for this purpose. It is *vegetation.* This restoration of vitiated air, I conjecture, is effected by plants imbibing the phlogistic matter with which it is overloaded by the burning of inflammable bodies. But whether there be any foundation for this conjecture or not, the fact is, I think, indisputable. I shall introduce the account of my experiments on this subject, by reciting some of the observations which I made on the growing of plants in confined air, which led to this discovery.

---

[6] Priestley, J. *Experiments and observations on different kinds of air.* London: J. Johnson, 4 vols., 1774-1777, xxiv, pp., 2 l.+324 pp., (pp. 43-44, 50-51, 51-52, 53-54). Priestley published his observations on air in several parts, with the result that the complete set of the first editions of the several contributions is difficult to obtain. When the first two volumes had been sold, second editions of these were printed to appear with the first edition of the third volume, etc. The selection above is taken from the first volume of the first edition and the pagination refers to this (see fig. 24).

One might have imagined that, since common air is necessary to vegetable, as well as to animal life, both plants and animals had affected it in the same manner; and I own I had that expectation, when I first put a sprig of mint into a glass-jar, standing inverted in a vessel of water: but when it had continued growing there for some months, I found that the air would neither extinguish a candle, nor was it at all inconvenient to a mouse, which I put into it.

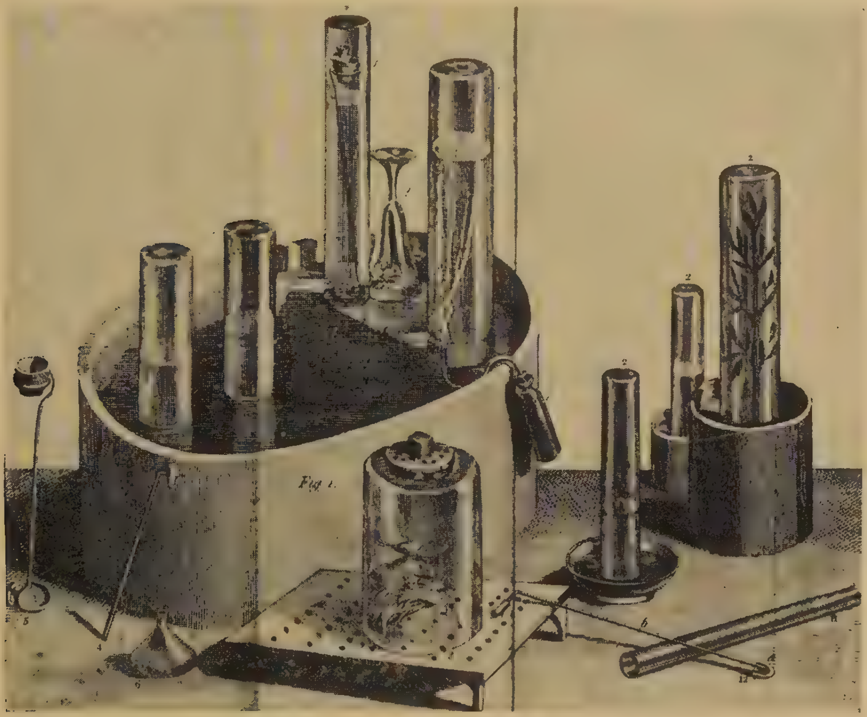


FIGURE 25. The frontispiece of the first edition of Priestley's *Experiments and observations upon different kinds of air*, 1774, showing some of the receivers in which he collected air. Mice are to be seen in the receiver number 3.

The plant was not affected any otherwise than was the necessary consequence of its confined situation; for plants growing in several other kinds of air, were all affected in the very same manner. . . .

Finding that candles burn very well in air in which plants had grown a long time, and having had some reason to think, that there was something attending vegetation, which restored air that had been injured by respiration, I thought it was possible that the same process might also restore the air that had been injured by the burning of candles.

Accordingly, on the 17th of August 1771, I put a sprig of mint into a quantity of air, in which a wax candle had burned out, and found that, on the 27th of the same month, another candle burned perfectly well in it. This experiment I repeated, without the least variation in the event, not less than eight or ten times in the remainder of the summer. . . .

This restoration of air, I found, depended upon the *vegetating state* of the plant; for though I kept a great number of the fresh leaves of mint in a small quantity of air in which candles had burned out, and changed them frequently, for a long space of time, I could perceive no melioration in the state of the air.

This remarkable effect does not depend upon any thing peculiar to *mint,* which was the plant that I always made use of till July 1772; for on the 16th of that month, I found a quantity of this kind of air to be perfectly restored by sprigs of *balm,* which had grown in it from the 7th of the same month.

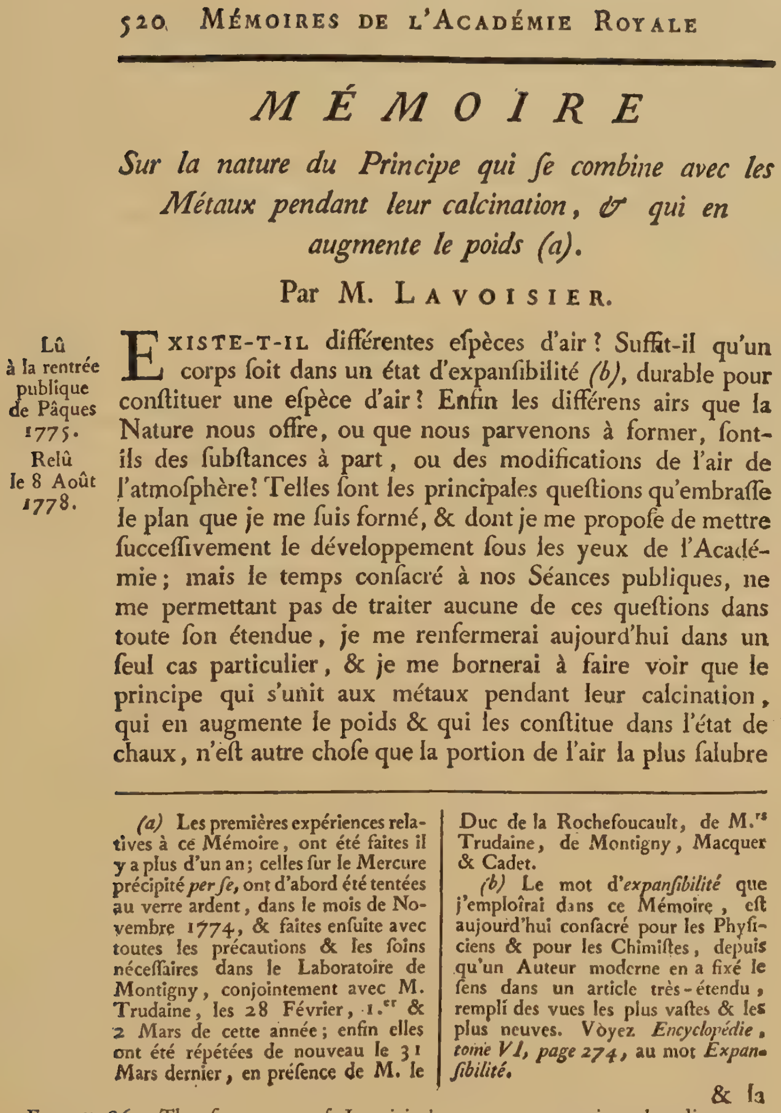
ANTOINE-LAURENT LAVOISIER

Antoine-Laurent Lavoisier (1743-1794), the discoverer of oxygen and of its importance in respiration, was a martyr of the French Revolution. "It took but a moment to cut off that head," said Lagrange, "though a hundred years, perhaps, will be required to produce another like it." Through the use of quantitative methods Lavoisier was able to overthrow the doctrines of phlogiston and to establish the elemental character of the gas which previously had been isolated by Mayow, Priestley and Scheele; and with a few poignant phrases he outlined the great facts of respiration: absorption of oxygen through the lungs with liberation of carbon dioxide ("fixed air"). He also gave conviction to the then unproved suspicion that respiration of living bodies was analogous to combustion, and that both resulted from union with oxygen of the air; we therefore heartily concur in Sir Michael Foster's conclusion that "he and he alone discovered oxygen." Of Lavoisier's first paper[7] of 1775 (see fig. 26) only the paragraph is included, which contains his conclusions. It is in a second contribution[8] that Lavoisier defines respiration. The selections from this paper are from the translation[9] of Thomas Henry of Warrington, a collaborator of Priestley, who at times clings to the terminology of the phlogistic doctrine.

[7] Lavoisier, A-L. "Mémoire sur la nature du principe qui se combine avec les métaux pendant leur calcination, & qui en augmente le poids." *Hist. Acad. roy. des Sciences,* 1775 Paris, 1778, pp. 520-526.

[8] Lavoisier, A-L. "Expériences sur la respiration des animaux, et sur les changemens qui arrivent à l'air en passant par leur poumon." *Hist. Acad. roy. des Sciences,* 1777, Paris, 1780, pp. 185-194.

[9] Henry, T. *Essays, on the effects produced by various processes on atmospheric air; with a particular view to an investigation of the constitution of the acids. By M. Lavoisier.* Warrington: W. Eyres, 1783 (pp. 1, 2-3, 10-12, 13-16).



520 MÉMOIRES DE L'ACADÉMIE ROYALE

MÉMOIRE

Sur la nature du Principe qui ſe combine avec les Métaux pendant leur calcination, & qui en augmente le poids (a).

Par M. LAVOISIER.

Lû
à la rentrée
publique
de Pâques
1775.
Relû
le 8 Août
1778.

EXISTE-T-IL différentes eſpèces d'air ? Suffit-il qu'un corps ſoit dans un état d'expanſibilité *(b)*, durable pour conſtituer une eſpèce d'air ? Enfin les différens airs que la Nature nous offre, ou que nous parvenons à former, ſont-ils des ſubſtances à part, ou des modifications de l'air de l'atmoſphère ? Telles ſont les principales queſtions qu'embraſſe le plan que je me ſuis formé, & dont je me propoſe de mettre ſucceſſivement le développement ſous les yeux de l'Académie; mais le temps conſacré à nos Séances publiques, ne me permettant pas de traiter aucune de ces queſtions dans toute ſon étendue, je me renfermerai aujourd'hui dans un ſeul cas particulier, & je me bornerai à faire voir que le principe qui s'unit aux métaux pendant leur calcination, qui en augmente le poids & qui les conſtitue dans l'état de chaux, n'eſt autre choſe que la portion de l'air la plus ſalubre

---

(a) Les premières expériences relatives à ce Mémoire, ont été faites il y a plus d'un an; celles ſur le Mercure précipité *per ſe,* ont d'abord été tentées au verre ardent, dans le mois de Novembre 1774, & faites enſuite avec toutes les précautions & les ſoins néceſſaires dans le Laboratoire de Montigny, conjointement avec M. Trudaine, les 28 Février, 1.^{er} & 2 Mars de cette année; enfin elles ont été répétées de nouveau le 31 Mars dernier, en préſence de M. le Duc de la Rochefoucault, de M.^{rs} Trudaine, de Montigny, Macquer & Cadet.

(b) Le mot d'*expanſibilité* que j'emploîrai dans ce Mémoire, eſt aujourd'hui conſacré pour les Phyſiciens & pour les Chimiſtes, depuis qu'un Auteur moderne en a fixé le ſens dans un article très-étendu, rempli des vues les plus vaſtes & les plus neuves. Voyez *Encyclopédie, tome VI, page 274,* au mot *Expanſibilité.*

& la

FIGURE 26. The first page of Lavoisier's paper announcing the discovery of oxygen (*Hist. Acad. des Sciences,* Paris, 1775, p. 520).

ON THE NATURE OF THE SUBSTANCE WHICH COMBINES WITH METALS DURING CALCINATION AND INCREASES THEIR WEIGHT

It seems proved that the substance which combines with metals during calcination, thereby increasing their weight, is none other than the purest part of the air surrounding us which we breathe, and which passes during this process from a state of elasticity to that of fixation. If therefore this result can be obtained of fixed air [carbon dioxide] whenever charcoal is used in the reduction of metals, the consequent increase of weight is due to the combination of charcoal with the pure part of the air and it is very probable that the calces, not only of mercury but of all metals would yield only highly respirable air, if they could be reduced like mercury, which becomes precipitated *per se.*

Since charcoal disappears completely during the revivifying of mercury calx and there remain after the process only mercury and fixed air it follows that the substance which has hitherto been called fixed air [carbon dioxide] results from a combination of the highly respirable air and charcoal. I propose to develop this conclusion more thoroughly in a series of further notes.

EXPERIMENTS ON THE RESPIRATION OF ANIMALS,

And on the Changes Effected on the Air in Passing Through Their Lungs

Of all the phenomena of the animal Economy, none is more striking, none more worthy the attention of philosophers and physiologists than those which accompany respiration. Little as our acquaintance is with the object of this singular function, we are satisfied that it is essential to life, and that it cannot be suspended for any time, without exposing the animal to the danger of immediate death. . . . .

The experiments of some philosophers, and especially those of Messrs. Hales and Cigna, had begun to afford some light on this important object; and, Dr. Priestley has lately published a treatise, in which he has greatly extended the bounds of our knowledge; and has endeavoured to prove, by a number of very ingenious, delicate, and novel experiments, that the respiration of animals has the property of phlogisticating air, in a similar manner to what is effected by the calcination of metals and many other chemical processes; and that the air ceases not to be respirable, till the instant when it becomes surcharged, or at least saturated, with phlogiston.

However probable the theory of this celebrated philosopher may, at first sight, appear; however numerous and well conducted may be the experiments by which he endeavours to support it, I must confess I have found it so contradictory to a great number of phenomena, that I could not but entertain some doubts of it. I have accordingly proceeded on a different plan, and have found myself led irresistibly, by the consequences of my experiments, to very different conclusions.

Now air which has served for the calcination of metals, is, as we have already seen, nothing but the mephitic residuum of atmospheric air, the highly respirable part of which has combined with the mercury, during the calcination: and the air which has served the purposes of respiration, when deprived of the fixed air, is exactly the same; and, in fact, having combined, with the latter residuum, about ¼ of its bulk of dephlogisticated air, extracted from the calx of mercury, I re-established it in its former state, and rendered it equally fit for respiration, combustion, &c. as common air, by the same method as that I pursued with air vitiated by the calcination of mercury.

The result of these experiments is, that to restore air that has been vitiated by respiration, to the state of common respirable air, two effects must be produced: 1st. to deprive it of the fixed air [carbon dioxide] it contains, by means of quicklime or caustic alkali: 2dly. to restore to it a quantity of highly respirable or dephlogisticated air, equal to that which it has lost. Respiration, therefore, acts inversely to these two effects, and I find myself in this respect led to two consequences equally probable, and between which my present experience does not enable me to pronounce. . . . .

The first of these opinions is supported by an experiment which I have already communicated to the academy. For I have shewn in a memoir, read at our public Easter meeting, 1775, that dephlogisticated air [oxygen] may be wholly converted into fixed air by an addition of powdered charcoal; and, in other memoirs, I have proved that this conversion may be effected by several other methods: it is possible, therefore, that respiration may possess the same property, and that dephlogisticated air, when taken into the lungs, is thrown out again as fixed air. . . . . Does it not then follow, from all these facts, that this pure species of air has the property of combining with the blood, and that this combination constitutes its red colour. But whichever of these two opinions we embrace, whether that the respirable portion of the air combines with the blood, or that it is changed into fixed air in passing through the lungs; or lastly, as I am inclined to believe, that both these effects take place in the act of respiration, we may, from facts alone, consider as proved:

1st. That respiration acts only on the portion of pure or dephlogisticated air, contained in the atmosphere; that the residuum or mephitic part is a merely passive medium which enters into the lungs, and departs from them nearly in the same state, without change or alteration.

2dly. That the calcination of metals, in a given quantity of atmospheric air, is effected, as I have already often declared, only in proportion as the dephlogisticated air, which it contains, has been drained, and combined with the metal.

3dly. That, in like manner, if an animal be confined in a given quantity of air, it will perish as soon as it has absorbed, or converted into fixed air, the major part of the respirable portion of air, and the remainder is reduced to a mephitic state.

4thly. That the species of mephitic air, which remains after the calcination of metals, is in no wise different, according to all the experiments I have made, from that remaining after the respiration of animals; provided always, that the latter residuum has been freed from its fixed air: that these two residuums may be substituted for each other in every experiment, and that they may each be restored to the state of atmospheric air, by a quantity of dephlogisticated air, equal to that of which they had been deprived. A new proof of this last fact is, that if the portion of this highly respirable air, contained in a given quantity of the atmospheric, be increased or diminished, in such proportion will be the quantity of metal which we shall be capable of calcining in it, and, to a certain point, the time which animals will be capable of living in it.

JOHN SCOTT HALDANE AND JOHN GILLIES PRIESTLEY

John Scott Haldane and John Gillies Priestley were the first to bring forward convincing evidence that the carbon-dioxide tension of the blood served as the normal stimulus for the respiratory centre. They proved that ventilation of the lungs normally depended upon the carbon-dioxide concentration of the alveolar air[10] and though at first they believed that this was the only factor, it was later pointed out that in certain circumstances oxygen-want may itself be an adequate cause of increased ventilation. The explanation of apnœa following forced breathing was a direct corollary to their observations upon the influence of carbon-dioxide tension.

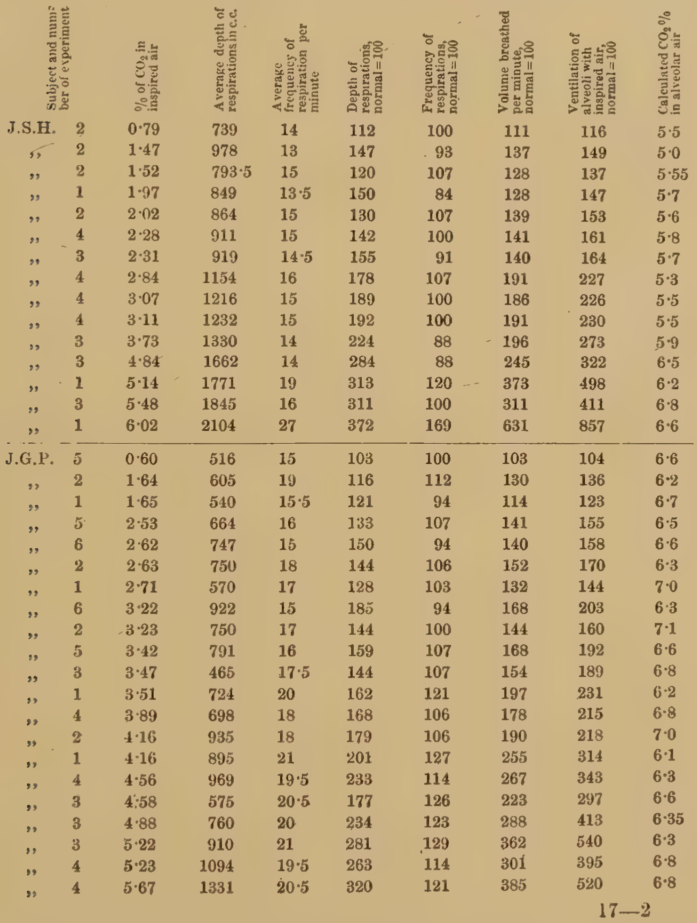
EFFECTS OF EXCESS OF CO_2 ON THE RESPIRATORY VENTILATION

For the purpose of studying the effects of CO_2 on the respiratory ventilation we placed the small box already described over the head of the subject in the plethysmograph. He thus breathed air in which the CO_2 produced by himself gradually accumulated. Samples of this air were taken at intervals with the precautions already described; and the depth and frequency of the respirations at the corresponding times were calculated from the corresponding parts of the tracing. Usually about four samples of air were taken during each experiment.

---

[10] Haldane, J. S. and J. G. Priestley. "Lung ventilation." *Jour. Physiol.*, vol. 32, pp. 225-266, 1905 (pp. 248, 249, 250, 252, 253, 254, 255).

The following table summarises the results obtained [Fig. 27]. As



Subject and number of experiment		% of CO_2 in inspired air	Average depth of respirations in c.c.	Average frequency of respiration per minute	Depth of respirations, normal = 100	Frequency of respirations, normal = 100	Volume breathed per minute, normal = 100	Ventilation of alveoli with inspired air, normal = 100	Calculated CO_2 % in alveolar air
J.S.H.	2	0·79	739	14	112	100	111	116	5·5
,,	2	1·47	978	13	147	93	137	149	5·0
,,	2	1·52	793·5	15	120	107	128	137	5·55
,,	1	1·97	849	13·5	150	84	128	147	5·7
,,	2	2·02	864	15	130	107	139	153	5·6
,,	4	2·28	911	15	142	100	141	161	5·8
,,	3	2·31	919	14·5	155	91	140	164	5·7
,,	4	2·84	1154	16	178	107	191	227	5·3
,,	4	3·07	1216	15	189	100	186	226	5·5
,,	4	3·11	1232	15	192	100	191	230	5·5
,,	3	3·73	1330	14	224	88	196	273	5·9
,,	3	4·84	1662	14	284	88	245	322	6·5
,,	1	5·14	1771	19	313	120	373	498	6·2
,,	3	5·48	1845	16	311	100	311	411	6·8
,,	1	6·02	2104	27	372	169	631	857	6·6
J.G.P.	5	0·60	516	15	103	100	103	104	6·6
,,	2	1·64	605	19	116	112	130	136	6·2
,,	1	1·65	540	15·5	121	94	114	123	6·7
,,	5	2·53	664	16	133	107	141	155	6·5
,,	6	2·62	747	15	150	94	140	158	6·6
,,	2	2·63	750	18	144	106	152	170	6·3
,,	1	2·71	570	17	128	103	132	144	7·0
,,	6	3·22	922	15	185	94	168	203	6·3
,,	2	3·23	750	17	144	100	144	160	7·1
,,	5	3·42	791	16	159	107	168	192	6·6
,,	3	3·47	465	17·5	144	107	154	189	6·8
,,	1	3·51	724	20	162	121	197	231	6·2
,,	4	3·89	698	18	168	106	178	215	6·8
,,	2	4·16	935	18	179	106	190	218	7·0
,,	1	4·16	895	21	201	127	255	314	6·1
,,	4	4·56	969	19·5	233	114	267	343	6·3
,,	3	4·58	575	20·5	177	126	223	297	6·6
,,	3	4·88	760	20	234	123	288	413	6·35
,,	3	5·22	910	21	281	129	362	540	6·3
,,	4	5·23	1094	19·5	263	114	301	395	6·8
,,	4	5·67	1331	20·5	320	121	385	520	6·8

17—2

FIGURE 27. The table from Haldane and Priestley's paper on the influence of CO_2 on the respiratory centres (*Jour. Physiol.*, 1905, vol. 32, p. 249).

the normal respirations while the subject was breathing pure air were also recorded at the beginning of each experiment, it was possible to calculate for each observation the increase in the depth and frequency of the respirations; and the results of these calculations are shown in separate columns. In calculating the alveolar ventilation, which is shown in one of the columns, we assumed a dead space of 190 c.c. for J.S.H. and 140 c.c. for J.G.P. (see above). The last column shows the calculated percentage of CO_2 in the alveolar air, assuming that the percentage at the beginning of the experiment was 5.6 for J.S.H., 6.3 for J.G.P., and that the respiratory exchange remained the same during the experiment.

It is quite evident from this table that the smallest increase in the CO_2 percentage of the air breathed is accompanied by a compensatory increase in the alveolar ventilation, the latter increase being just about sufficient to keep the alveolar CO_2 percentage constant. The results thus confirm those obtained by direct determinations of the CO_2 percentage in alveolar air while the subject was breathing air rich in CO_2 (see above). It will also be seen that the increased alveolar ventilation was at first almost entirely obtained by increased depth of the respirations, there being little or no alteration in their frequency until the alveolar ventilation had been increased to about five times the normal. Owing to the existence of the dead space this means of increasing the alveolar ventilation is evidently much more economical than a simple increase in the frequency would be, since, as the table shows, with increasing depth of respirations the alveolar ventilation increases more rapidly in proportion than the total respiratory ventilation. Mere observations of the frequency of respiration evidently afford no measure of the alveolar ventilation, and may be very misleading. It will be seen, for instance, that even when the alveolar ventilation was increased to three times the normal, there might be an actual diminution in the frequency of the respirations.

DISCUSSION OF RESULTS AND FURTHER EXPERIMENTS ON APNŒA

The experiments which have been detailed above indicate clearly that under normal conditions the regulation of the lung-ventilation depends on the pressure of CO_2 in the alveolar air. Even a very slight rise or fall in the alveolar CO_2 pressure causes a great increase or diminution in the lung ventilation. Thus we found that a rise of 0.2% of an atmosphere in the alveolar CO_2 pressure was sufficient to double the ventilation of the lung alveoli. For each individual the normal alveolar CO_2 pressure appears to be an extraordinarily sharply defined physiological constant.

By what paths do variations of the alveolar CO_2 pressure affect the respiratory centre? All the available evidence appears to us to point clearly to the conclusion that the arterial blood, and this alone, furnishes the connection. Against the existence of a nervous connection through the vagus or sympathetic, suggested originally by Marshall Hall, are the facts that, as shown by Geppert and Zuntz, hyperpnœa occurs as usual, and in the same degree, whether or not the vagus and sympathetic have first been cut, and whether or not the nervous connections between the active muscles and the respiratory centre have been severed.

There is clear positive evidence that the blood is itself a carrier to the respiratory centre of stimuli which produce hyperpnœa. The most striking proof has been furnished by Fredericq, who showed that apnœa is produced in an animal whose respiratory centre is supplied with arterial blood from a second animal to which artificial respiration is applied. The previous experiments of Geppert and Zuntz on this point are equally convincing. Hence, assuming that CO_2 is the normal stimulus to the respiratory centre, there is no room for doubt that it is through a rise in the CO_2 pressure of the blood supplying the centre that the stimulus is furnished.

Normal hyperpnœa, such as that due to muscular work, may be explained as follows. The venous blood, returning to the lungs in larger quantity, and probably also more highly charged with CO_2, causes a rapid rise in the alveolar CO_2 pressure, and consequent rise in the arterial CO_2 pressure. The respiratory centre is thus stimulated to increased activity, with consequent lowering of the alveolar CO_2 pressure, until a point is struck at which an equilibrium is maintained between the effect of the increased supply of venous blood in raising the arterial CO_2 pressure and that of the increased respiratory activity in lowering it.

For "chemical" apnœa (as distinguished from "vagus" or "distention" apnœa, if such a thing exists) the following explanation seems to agree with the facts recorded by previous observers and by ourselves. The forced or artificial respiration causing the apnœa lowers the CO_2 pressure in the alveolar air and consequently in the arterial blood. The consequence is that CO_2 is washed out of the centre, and the CO_2 pressure in its cells is lowered below the threshold value at which activity of the centre begins. Not only so, but CO_2 is washed out of the tissues of the body generally, so that even the venous blood may have a lower CO_2 tension than corresponds to the threshold value for the respiratory centre; and blood which is quite dark in colour may thus fail to excite the centre. As a consequence it will be a considerable time after the forced or artificial respiration has ceased before the CO_2 pressure in the cells of the respiratory centre again arises to the threshold value; and it may happen that the centre is first again actually excited, not by CO_2, but by deficiency of oxygen.

YANDELL HENDERSON

Yandell Henderson, the Professor of Applied Physiology at Yale University, carried out important investigations upon the physiology of respiration, especially in relation to clinical medicine, and upon the volume output of the heart. His early experiments upon acapnia focussed the attention of physiologists upon this important problem and as a result of his observations, Henderson was led to recommend the administration of carbon dioxide in conditions of shock, *e.g.*, from anæsthesia, drowning and carbon monoxide poisoning. The report of his first experiments, read in May 1907, is given in full below.[11] This was followed between 1907 and 1911 by a series of significant papers on acapnia which appeared in the *American Journal of Physiology*. In the fourth paper of the series Henderson showed that fatal apnœa might follow excessive forced breathing,[12] and in the sixth paper the relation of acapnia to anæsthesia was first pointed out and the inhalation of carbon dioxide recommended as a means of combating collapse due to anæsthesia.[13]

PRODUCTION OF SHOCK BY LOSS OF CARBON DIOXIDE, AND RELIEF BY PARTIAL ASPHYXIATION

The writer is led by a large number of experiments to advance the following hypothesis to explain the causation of shock by extreme pain: Pain induces violent and prolonged hyperpnœa. The carbon dioxide content, not only of the arterial blood but of the tissues of the body as well, is thus greatly reduced. This condition of acapnia lowers the tonus of the peripheral blood vessels, and induces tachycardia, shallow respiration, failure of reflexes, and the mental condition characteristic of surgical shock.

The liability to shock which attaches to the exposure of the abdominal viscera is to be explained by the exhalation of carbon dioxide from the organs exposed, and the consequent loss of tonus in their blood vessels.

---

[11] Henderson, Y. "Production of shock by loss of carbon dioxide, and relief by partial asphyxiation." *Amer. Jour. Physiol.*, vol. 18, (Proc.), pp. xi-xix, 1907.

[12] Henderson, Y. "Acapnia and shock.—IV. Fatal apnœa after excessive respiration." *Amer. Jour. Physiol.*, vol. 25, pp. 310-333, 1910.

[13] Henderson, Y. and M. M. Scarbrough. "Acapnia and shock.—VI. Acapnia as a factor in the dangers of anæsthesia." *Amer. Jour. Physiol.*, vol. 26, pp. 260-286, 1910.

Thus it was found that when a loop of intestine of a cat was exposed to a current of air warmed to 35° to 38° C. and saturated with moisture, an extreme congesion rapidly developed. When the loop was placed in saline saturated with carbon dioxide, the congestion rapidly disappeared. When the abdominal viscera of a dog under moderate anæsthesia were thus exposed for one hour, and moderate hypernœa was thereafter induced for ten minutes by stimulation of the sciatic nerve, shock developed. Arterial pressure fell to 60 mm. Respiration was very shallow. The animal was comatose, and wholly insensitive to stimulation of afferent nerves.

Rapid recovery was effected by assisting in the restoration of the normal carbon dioxide content of the body. The dead space of the respiratory tract was increased by attaching to the trachea a piece of hose a metre in length and 2 cm. in diameter. A moderate volume of saline saturated with carbon dioxide was perfused into the femoral vein. Within fifteen minutes arterial pressure had risen above 160 mm. Respiration was full and deep. The animal came out of the coma, and the reactions to sensory stimuli were restored to normal character and intensity.

All of the above quoted experiments have been performed repeatedly.

JOSEPH BARCROFT

Joseph Barcroft, Professor of Physiology at Cambridge, is well-known for his studies upon the dissociation curves of hæmoglobin and more recently for his analysis of the functions of the spleen. Barcroft has been one of those who have stoutly maintained the belief that the exchange of substances through the epithelium of the lungs and the tissues occurs by virtue of the simple process of diffusion, and he has obtained strong experimental evidence in favour of this dogma. Not the least significant step in his argument came from his studies upon the effect of altitude. His powers of logical analysis, set forth in singularly attractive language, are nowhere, it seems to me, better illustrated than in the following passage from the second edition of his well-known monograph.[14] The first two paragraphs of his original preface have also been included.

PREFACE

At one time, which seems too long ago, most of my leisure was spent in boats. In them I learned what little I know of research, not of technique or of physiology, but of the qualities essential to those who would venture beyond the visible horizon.

---

[14] Barcroft, J. *The respiratory function of the blood.* Cambridge: University Press, x+320 pp., 1914 (p. vii); 2nd edition, part 1, xii+207 pp., 1925 (pp. 88, 89, 90-91).

The story of my physiological "ventures" will be found in the following pages. Sometimes I have sailed single handed, sometimes I have been one of a crew, sometimes I have sent the ship's boat on some expedition without me. Any merit which attaches to my narrative lies in the fact that it is in some sense at first hand. I have refrained from discussing subjects which I have not actually touched, but which might fittingly have been included in a modern account of the blood as a vehicle for oxygen. Such are the relation of narcosis to oxygen-want and the properties of intracellular oxidative enzymes. The omission of these and other important subjects has made the choice of a title somewhat difficult. I should like to have called the book, what it frankly is—a log; did not such a title involve an air of flippancy quite out of place in the description of the serious work of a man's life. I have therefore chosen a less exact, though more comprehensive title.

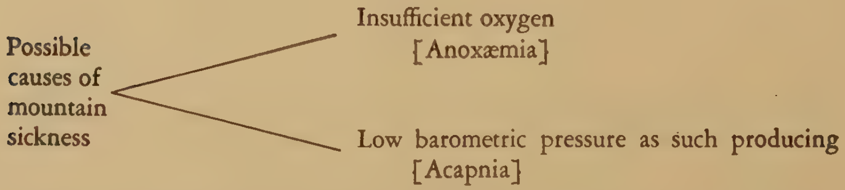
Chapter VII

THE HYDROGEN-ION CONCENTRATION OF THE BLOOD

After this somewhat lengthy digression let me return to the subject of mountain sickness. I had mentioned that the symptoms were attributed by Paul Bert to an actual want of sufficient molecules of oxygen in each cubic foot of air inspired into the lungs. This view of the matter was not allowed to go unchallenged for long. Mosso, who, as I have said, was the great moving force in the study of high altitudes, put forward a rival theory, based on the fact that the expired air contained less carbonic acid at high altitudes than at the sea-level.

The position then at the end of Mosso's life may be briefly stated in the following table:

Scheme 1

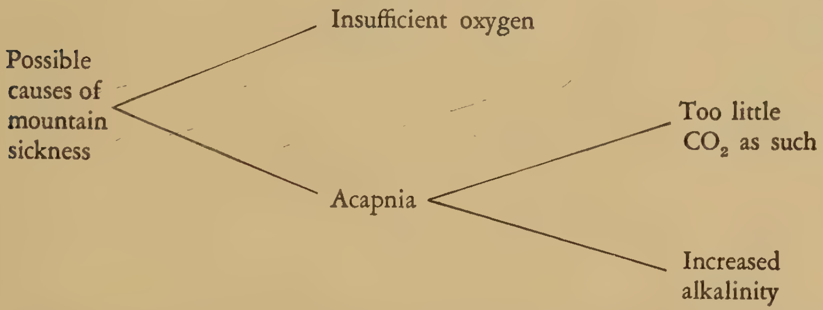

Possible causes of mountain sickness
Insufficient oxygen
[Anoxæmia]
Low barometric pressure as such producing
[Acapnia]

Granting the possibility of the existence of acapnia, the further question would arise: How does the acapnia produce its supposed results?

There are two possible ways in which it might be held to act. The first is that the absence of CO_2 *per se* should affect the functions of the body, the second is that other things being equal the evaporation of CO_2 from the blood would render that fluid more alkaline. This alkalinity would be reflected by the tissues generally and might affect their function.

The table which I have given above as expressing the causes of mountain sickness then might be expanded as follows and the alternatives then would be:

SCHEME 2

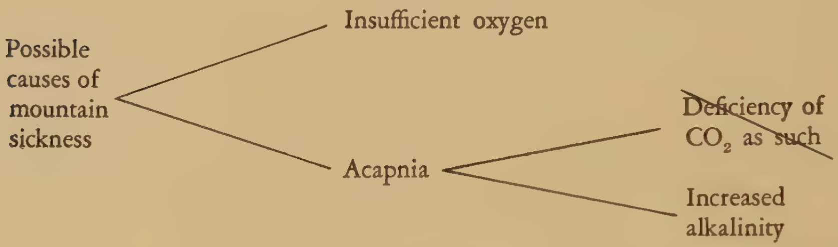

Insufficient oxygen
Possible causes of mountain sickness
Too little CO_2 as such
Acapnia
Increased alkalinity

Such then was the position when the subject became one of first hand interest to me. In 1909 the late Professor Zuntz of Berlin sent me a very pleasant invitation. It contained the news that he was about to organize an expedition to Teneriffe the following year. This expedition was to be international in character and he asked me to accompany him and to bring another English worker with me. I was fortunate in having Dr. Douglas as my colleague. The results which we brought back from Teneriffe shed some light on each of the possible mechanisms of acapnia. Let us first consider whether or not the mere reduction of CO_2, as such, in the blood is responsible for mountain sickness.

	Pressure of CO_2 in alveolar air mm.		
	Sea Level Europe	*Cañadas*	*Alta Vista*
Douglas	41	36	32
Barcroft	40	41	38
Zuntz	35	29	27

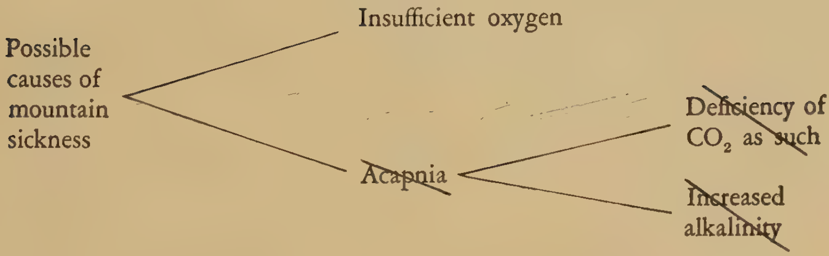
The above table shows that as between the sea-level and the Alta Vista Hut, there was a drop of more than 20 per cent. in the alveolar CO_2 tensions of Zuntz and Douglas. There was no such drop in my case. The drop of 7 or 9 mm. in the alveolar CO_2 is caused of course by increased total ventilation on their parts, as a corollary to which there was a corresponding rise in alveolar oxygen. Zuntz and Douglas have alveolar oxygen pressures of some ten millimetres above my own. Now if reduced CO_2 pressure were the cause of mountain sickness Zuntz and Douglas should have been the sufferers, if reduced oxygen pressure in the alveolar air were the cause I would be the victim, as, in fact, I was to some extent. This experiment was controlled on Monte Rosa where my carbonic acid pressure dropped in the ordinary way and where I did not suffer at all. I am prepared therefore to delete "reduction of CO_2 as such" from the scheme of possible causes of mountain sickness which now stands as follows:

SCHEME 3


Insufficient oxygen
Possible causes of mountain sickness
~~Deficiency of CO_2 as such~~
Acapnia
Increased alkalinity

Let us now turn to another possibility which the acapnia theory presents, namely that of decreased alkalinity of the blood. On our return from Teneriffe I was quite of the opinion that it might be deleted as well. The argument was as follows. The affinity of haemoglobin for oxygen depends upon the circumstances under which the haemoglobin is placed, it decreases with a rise of temperature, with a rise in hydrogen-ion concentration, and it is also influenced by salts. Small additions of salt to blood do not however produce any appreciable effect on the affinity of the haemoglobin for oxygen. On the other hand, small changes in hydrogen-ion concentration do produce a very marked effect. At constant temperature then my idea was that if the alkalinity of the blood increased the haemoglobin would gain in its affinity for oxygen to an extent which might be discernible. This matter was tested on the bloods of each member of the party. As the result of these tests it appeared that when the blood, drawn at any given altitude was exposed to any standard pressure of oxygen, in the presence of the concentration of carbonic acid which the actual blood contained in the body at that altitude. Scheme 3 then turned into Scheme 4.

SCHEME 4


Insufficient oxygen
Possible causes of mountain sickness
~~Acapnia~~
~~Deficiency of CO_2 as such~~
~~Increased alkalinity~~

FREDERICK GOWLAND HOPKINS

SIR FREDERICK GOWLAND HOPKINS, the Professor of Biochemistry at Cambridge, has been associated with three great developments in modern physiology. In 1906 he began his experiments on the importance of accessory factors in a normal diet, which culminated in the discovery of the vitamins; at about the same time, in collaboration with Sir Walter Morley Fletcher, he undertook the chemical analysis of muscular activity, establishing for the first time the importance of lactic acid; finally, he has recently discovered glutathione, a respiratory enzyme of the tissues, which has shed highly significant light upon the metabolic processes occurring peripherally.[15]

GLUTATHIONE

The research described in this paper, though its actual point of departure had an intention quite different,[16] ultimately resolved itself into an endeavour to throw light upon the chemical nature and physiological significance of a constituent of living tissues, which, though hitherto of unknown nature, has long carried a name. There can scarcely be a doubt that the substance to be described is the "Philothion" of de Rey-Pailhade.

In 1888 this author showed that yeast cells and aqueous extracts of yeast have the property of reducing sulphur to hydrogen sulphide [de Rey-Pailhade, 1888]. Later he showed that many animal tissues possess the same property. Throughout a long series of communications upon the subject he has courageously maintained the view that the labile hydrogen thus shown to exist in living cells has important respiratory functions. His views as to the probable nature of the hypothetical substance (named as above) which he supposed to carry this labile hydrogen, have been modified from time to time. In his latest writings he speaks of it as the hydride of a protein ("hydrure d'albumine"). After the publication of Heffter, to which reference will immediately be made, he accepted the view that the labile hydrogen exists in sulphydryl groups, HS—. . . . .

---

[15] Hopkins, F. G. "On the autoxidisable constituent of the cell." *Biochem. Jour.*, vol. 15, pp. 286-305, 1921 (pp. 286, 288, 303, 304).

[16] My attention was directed to the subject in two separate ways. Some years ago I was endeavouring to discover if vitamins were to be found among sulphur-containing compounds, and was led part of the way towards the separation of the substance now described. A little later, acting on the suggestion that acid formation in muscle is a necessary factor in contraction I wished to discover if by chance in the absence of carbohydrate, aceto-acetic acid from fat might function instead of lactic acid. This led me to apply the nitro-prusside test to tissues. At this time Arnold's papers had not yet appeared and I was ignorant of Heffter's publication. The above mentioned enquiries were nugatory but they led to the present one.

Section III

ISOLATION OF A DIPEPTIDE

Yeast has been chiefly used as a source of the substance to be described, but the same product has been obtained from mammalian muscle, and mammalian liver.

There was every reason in advance to expect that it would be found to have a very low concentration in the tissues. As already stated, the nitroprusside reaction is extremely delicate, and tissue extracts when completely freed from proteins contain only very small amounts of organic sulphur. The actual yield of H_2S when yeast cells or animal tissues are treated with sulphur (supposing this to measure sulphydryl groups with any accuracy) is minute.

The discovery of a method of isolation cost much labour; but could the nature and properties of the substance have been known in advance, greater difficulties might well have been expected. . . . .

The following shows the acceleration of reduction due to the addition of oxidised dipeptide to the system in neutral or slightly alkaline conditions. The solution in each case was a phosphate buffer solution, the P_h being adjusted after the addition of the dipeptide. Chloroform was added to all the tubes and there was a layer of toluene on the surface. The tubes were filled with nitrogen.

Tissue preparation	*Buffer solution*	*Methylene blue*	*Oxidised dipeptide added*	P_h	*Reduction time*
0.2 g.	5 cc.	0.5 cc.	0 mg.	7.4	5 hrs. 45 mins.
0.2 g.	5 cc.	0.5 cc.	4 mg.	7.4	2 hrs. 40 mins.
0.2 g.	5 cc.	0.5 cc.	0 mg.	7.8	3 hrs. 45 mins.
0.2 g.	5 cc.	0.5 cc.	4 mg.	7.8	1 hr. 40 mins.
0.5 g.	5 cc.	0.5 cc.	0 mg.	7.8	2 hrs. 30 mins.
0.5 g.	5 cc.	0.5 cc.	4 mg.	7.8	0 hr. 55 mins.

The conditions can be adjusted to give more rapid reduction and sharper contrasts than the above.

Tissue	*Buffer solution*	*Methylene blue*	*Oxidised dipeptide*	P_h	*Reduction time*
Liver .15 g.	5 cc.	0.3 cc.	4 mg.	7.4	0 hr. 25 mins.
Liver .15 g.	5 cc.	0.3 cc.	0 mg.	7.4	6 hrs. +
Muscle (washed) 0.2 g. . .	5 cc.	0.3 cc.	8 mg.	7.4	0 hr. 10 mins.
Muscle (washed) 0.2 g. . .	5 cc.	0.3 cc.	0 mg.	7.4	3 hrs. +

It seems clear that in the reactions described the -S-S- group of the oxidised dipeptide acts first as a hydrogen acceptor and under conditions of even slight acidity the resulting HS- groups are too stable to transfer the hydrogen to another acceptor. In neutral or slightly alkaline solution on the other hand the hydrogen is transferred to the methylene blue. If this view be the right one we have to recognise the important fact that the two reactions involved in the transference of hydrogen to the disulphide group under the influence of a tissue enzyme, and its subsequent transference from sulphydryl groups to the methylene blue acceptor, together run faster than the single reaction in which the dye is directly reduced by the tissue enzyme. The dipeptide then possesses what are essentially catalytic properties and would be fairly spoken of as a co-enzyme. Indeed, if tissues are very thoroughly washed, as in the observations of Thunberg referred to earlier, so that their power to reduce methylene blue is practically removed, the restoration of this power when the oxidised dipeptide is added at once gives the impression that it has the function of a co-ferment exerted on the lines suggested. . . . .

SUMMARY

A substance responsible for the nitroprusside reaction which is given by nearly all animal tissues, and was applied by Heffter and by Arnold in proof of the presence of sulphydryl groups in the cell, has been isolated from yeast, from muscle, and from mammalian liver. It has the properties of the philothion of de Rey Pailhade.

Evidence is given to show that the substance is a dipeptide containing glutamic acid and cysteïn. The relation of the two amino-acids in the molecule has not yet been determined. Though present in low concentration (0.01 to 0.02% of the fresh tissue) the dipeptide contains practically the whole of the non-protein organically bound sulphur of the cell.

The substance is autoxidisable, and, owing to the changes in the sulphur group of its cysteïn moiety from the sulphydryl to the disulphide condition and *vice versa,* it acts readily under varying conditions either as a hydrogen acceptor or an oxygen acceptor (hydrogen "donator"). It can be both reduced and oxidised under the influence of factors shown to be present in the tissues themselves.

Evidence is discussed which suggests that the substance has actual functions in the chemical dynamics of the cell.

CHAPTER V

DIGESTION

K*NOWLEDGE* of the physiology of digestion naturally had to await the rise of modern chemistry, and in the early period one encounters speculations which reflect the alchemical vagaries of the age. The term "fermentation" was used to describe the changes which occur in the stomach, but the word was of uncertain connotation and writers of the 16th and 17th centuries confused each other by refusing to define this and many other terms which they used. The first contribution which sounded a modern note was that of the Venetian Sanctorius Sanctorius who performed the simple experiment of weighing a human being (himself) before and after a meal, and found that he increased in weight by the amount which he had eaten. Sylvius de le Boë and Van Helmont speculated concerning digestion, but it remained for Sylvius's youthful pupil, Regnier de Graaf, to perform one of the first significant experiments in the history of gastric physiology. He isolated the pancreatic duct in a dog and, by making a permanent fistula, was able, in 1664, to collect the pancreatic juice. After de Graaf the next observations of importance are those of Réaumur on the properties of the gastric juice of birds. Spallanzani established for human gastric juice properties similar to those which Réaumur had found for birds. Like many enquirers after truth, Spallanzani performed the human experiment with himself as subject. The correlation of gastric physiology with chemistry did not begin, however, until Prout had found that the human stomach contained hydrochloric acid (1824). A few years later (1835) Schwann isolated pepsin. Meanwhile William Beaumont had begun his remarkable observations upon Alexis St. Martin; once more human experiment led to a far-reaching advance in knowledge of physiological processes. It is probably true that Beaumont carried out his observations without knowledge of what had been done before him, and that his discoveries were therefore arrived at independently of his predecessors. However, he gives an excellent historical discussion in his book, but one suspects that this was prepared at the time the book was being written, while the observations had been made long before. The modern developments which have come through the now classical experiments of Pavlov, Cannon, Bayliss and Starling need no special comment except that their discoveries have been complete in themselves, and little of significance has been added to the evidence which they presented in their original descriptions.

SANCTORIUS SANCTORIUS

Sanctorius Sanctorius (1561-1636), Professor of Medicine at Padua, well known in the history of medicine for his clinical thermometer and pulse-clock, had an enquiring mind and considerable mechanical ingenuity. He devised instruments for extracting stones from the bladder and foreign bodies from the external auditory meatus. His contribution to physiology lay in his observations upon insensible perspiration, by which he founded the science of metabolism. He had constructed a chair suspended from a steelyard which, used as a balance, made possible accurate determinations of body weight at various times, before and after eating, sleeping and the execution of other physiological functions. As Foster points out, he nowhere described his experiments, merely the conclusions were given and these in the form of a series of several hundred brief aphorisms,[1] a selection from which is given below from John Quincy's 18th century translation.[2]

MEDICINA STATICA

Sect. 1

OF INSENSIBLE PERSPIRATION, AS IT APPEARS BY WEIGHT

Aphorism I. If there daily be an Addition of what is wanting, and a Subtraction of what abounds, in due Quantity and Quality, lost Health may be restor'd, and the present preserv'd.

Aph. II. If a Physician who has the Care of another's Health, is acquainted only with the sensible Supplies and Evacuations, and knows nothing of the Waste that is daily made by Insensible Perspiration, he will only deceive his Patient, and never cure him.

Aph. III. He only who knows how much, and when the Body does more or less insensibly perspire, will be able to discern, when, and what is to be added or taken away, either for the Recovery or Preservation of Health.

---

[1] Sanctorius, S. *Ars Sanctorii Sanctorii. De statica medicina, aphorismorum sectionibus septem comprehensi. Accesit staticomostix sive ejusdem artis demolitio Hippolyti Obicii.* Venice: 1614.

[2] The first edition of John Quincy's translation appeared under the following title: *Medicina statica: being the aphorisms of Sanctorius translated into English with large explanations. . . .* London: William Newton, lvi+311 pp., 1712 (pp. 1-12; 117; 175).

Aph. IV. Insensible Perspiration alone, discharges much more than all the sensible Evacuations together.

Aph. V. Insensible Perspiration, is either made by the Pores of the Body, which is all over Perspirable and covered with a Skin like a Nett; or it is performed by Respiration through the Mouth, which usually in the space of one Day amounts to about the quantity of half a Pound, as may plainly be made appear by breathing upon a Glass.

Aph. VI. If eight Pounds of Meat and Drink are taken in one Day, the Quantity that usually goes off by Insensible Perspiration in that Time, is five pounds.

Aph. VII. The Quantities insensibly perspir'd, vary according to the Differences of Constitutions, Ages, Countries, Seasons, Distempers, Diet, and the rest of the Non-naturals.

Aph. VIII. If the Body be weighed in the Morning before and after Sensible Evacuation, then it will be easie to determine the Quantity that is wasted that Night by Perspiration.

Aph. IX. If the Body encreases beyond its usual Weight without Eating or Drinking more than customary, there must either be a Retension of some of the sensible Excrements, or an Obstruction of the Perspirable Matter.

Aph. X. The Body continues in the same State of Health, as long as it returns to its wonted Weight, without any increase of the sensible Evacuations: But if it comes to its Standard by larger Discharges, either by Stool or Urine, than ordinary, it then begins to decline from its former Health.

Aph. XI. If by Weight it appears, that Perspiration is diminish'd; the following Days it must either be increased, or some sensible Evacuation enlarged; or else there will be laid a Foundation for a Cachexy, or a Fever.

Aph. XII. A larger Perspiration, and greater sensible Evacuations than usual, cannot be at the same time.

Aph. XIII. If any one sensibly evacuates more than he ought, at that time he perspires less.

Aph. XIV. To evacuate too much by Stool, Urine, or Sweat, and perspire less than usual is bad.

Aph. XV. If a Body returns to the same Standard every Day, without any change in the Quantity of Perspiration, there will be constantly preserved a perfect Health, and no need of Critical Evacuations.

Aph. XVI. Bad Qualities arise when the Body is not one Day the same in Weight as another.

Aph. XVII. A Person may certainly conclude himself in a State of Health if upon ascending a Precipice he finds himself more lightsome than before.

Aph. XVIII. From too great Fullness arise bad Qualities, but not, *vice versâ.*

Aph. XIX. Too great a weight and fullness may be lessen'd by Sensible or Insensible Evacuations, either of digested or undigested Matter, and it is good so to do; but although it lessens the Load, yet it leaves ill Qualities behind.

Aph. XX. There are two Kinds of Insensible Perspiration the one is during Sleep, of Humours that are well digested, and after which there is an increase of Strength: The other is when awake, and arises from indigested Humours, and is weakning more or less, according to the greater or lesser Actions of the Muscles during that Time.

Aph. XXI. That Perspiration which is beneficial, and most clears the Body of superfluous Matter, is not what goes off with Sweat, but that insensible Steam or Vapour, which in Winter time exhales to about the Quantity of Fifty Ounces in the space of one natural Day.

Aph. XXII. Insensible Perspiration becomes Visible, when there is too great a supply, or upon Faintings, or upon violent Motion.

Aph. XXIII. Insensible Perspiration accompany'd with Sweat is bad: Because Sweat diminishes the strength of the Fibres. 'Tis sometimes said to be serviceable, Because it diverts from a greater Evil.

Aph. XXIV. By how much the more subtile, and without apparent Moistness, Perspiration is made, it is by so much the more healthful.

Aph. XXV. All the thinner Excrements are the heaviest, and sink: The thick ones are lighter and swim, such as are the hard consistent Stools, the *Saliva,* and several others of the like Kind.

Aph. XXVI. The thin Secretions abate more the Weight of the Body in Proportion to their Quantities, than the hard and consistent.

Sect. III.

Aph. XI. A full or an empty Stomach, lessens Perspiration, for a full one diverts it by a Corruption of the Aliment; and an empty one draws it back that it may be filled.

Aph. XII. When a full Meal is not perfectly digested, it is to be

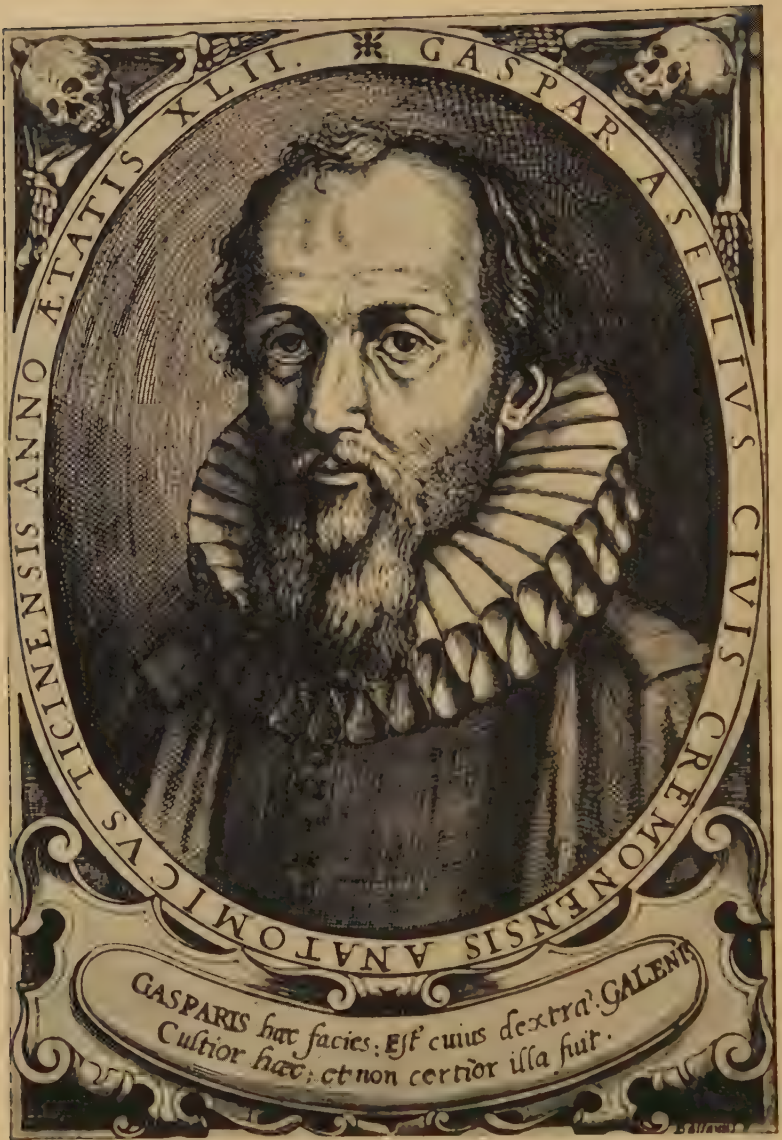

GASPAR ASELLIUS CIVIS CREMONENSIS ANATOMICUS TICINENSIS ANNO ÆTATIS XLII.
GASPARIS hæc facies: Est cuius dextra GALENI
Cultior hæc; et non certior illa fuit.

Figure 28. The Bassanus engraving of Aselli at the age of 42 which is to be found in a few copies of the "De lactibus", 1627.

known by an increase of Weight; for the Body will not then perspire well: But an empty Stomach is filled with Vapours.

Sect. IV.

Aph. XXIX. If five Hours after Supper, a Person is suddenly awakned, and weighed, he will be found to have perspired barely half a Pound; but if eight Hours after Supper, the same Experiment be tryed, three Pounds.

Aph. XXXI. By some Part of the usual Perspiration being retained, either the next Day after Dinner we fall asleep, and perspire in the Space of an Hour, about a Pound: or the following Night Sleep is so much the longer, by which more than usual is perspired: or else we fall into some sensible Crisis, or a Distemper.

GASPARO ASELLI

Gasparo Aselli (1581-1626), a Milanese surgeon and anatomist, discovered, apparently by accident, the structures now known as the lacteals. Their recognition represents an important milestone in the development of knowledge concerning nutrition. Aselli erroneously believed that the "lacteal veins" led to the liver and it was not until Jean Pecquet (1622-1674) discovered the thoracic duct and proved that its lower end, the receptaculum chyli, was continuous with the lacteals that their relation to the process of absorption became more clearly established. Foster's translation of Aselli's original description,[3] which is given below, can scarcely be improved upon.

THE LACTEALS

On the 23rd of July of that year (1622) I had taken a dog in good condition and well fed, for a vivisection at the request of some of my friends, who very much wished to see the recurrent nerves. When I had finished this demonstration of the nerves, it seemed good to watch the movements of the diaphragm in the same dog, at the same operation. While I was attempting this, and for that purpose had opened the abdomen and was pulling down with my hand the intestines and stomach gathered together into a mass, I suddenly beheld a great number of cords as it were, exceedingly thin and beautifully white, scattered over the whole of the mesentery and the intestine, and starting from almost innumerable beginnings. At first I did not delay, thinking them to be nerves. But presently I saw that I was mistaken in this since I noticed that the nerves belonging to the intestine were distinct from these cords, and wholly unlike them, and, besides, were distributed quite separately from them. Wherefore struck by the novelty of the thing, I stood for some time silent while there came into my mind the various disputes, rich in personal quarrels no less than in words, taking place among anatomists concerning the mesaraic veins and their function. And by chance it happened that a few days before I had looked into a little book by Johannes Costaeus written about this very matter. When I gathered my wits together for the sake of the experiment, having laid hold of a very sharp scalpel, I pricked one of those cords and indeed one of the largest of them. I had hardly touched it, when I saw a white liquid like milk or cream forthwith gush out. Seeing this, I could hardly restrain my delight, and turning to those who were standing by, to Alexander Tadinus, and more particularly to Senator Septalius, who was both a member of the great College of the Order of Physicians and, while I am writing this, the Medical Officer of Health, "Eureka" I exclaimed with Archimedes, and at the same time invited them to the interesting spectacle of such an unusual phenomenon. And they indeed were much struck with the novelty of the thing.

---

[3] Aselli, G. *De lactibus siue lacteis venis, quarto vasorum mesaraicorum genere, nouo inuento. Dissertatio qua sententiæ anatomicæ multæ uel parum perceptæ illustrantur. . . .* Mediolani: apud J. B. Bidellum, 10 pl. leaves, 79 pp., 4 col. plates, portrait, 1627. The plates accompanying this tract are the first coloured anatomical illustrations of importance in the history of bookmaking. The work was published posthumously through the generosity of that liberal patron of science, Nicholas de Pieresc. The engraving of Aselli (reproduced in Fig. 28), which is present in some copies of his book, was made in the 42nd year of his age, thus coinciding closely with his discovery of the lacteals (July 23rd, 1622).

REGNER DE GRAAF

Regner de Graaf (1641-1673), a brilliant young pupil of Sylvius de le Boë, carried out at the early age of 22 an important series of experiments on the physiology of the pancreas. He records that they were commenced in 1663, and they were published in the following year as a dissertation for his doctor's degree. He succeeded in introducing a temporary cannula, made of the quill of a wild duck, into the pancreatic duct of a living dog, and he studied the properties of the liquid so obtained, observing its clear colour, acid reaction, and bitter taste. De Graaf's account of his unsuccessful attempts to collect pancreatic juice, followed by his eventual success, is one of the most interesting passages in the history of the experimental method and is given below in full.[4]

---

[4] de Graaf, R. *Disputationum medicarum de natura et usu succi pancreatici.* Lugdunum Batavorum: Hackianna, 90 pp., 1 pl., 1664. A French translation appeared in Paris in 1666, and a second Latin edition with many additions to the text in 1671. An English edition,

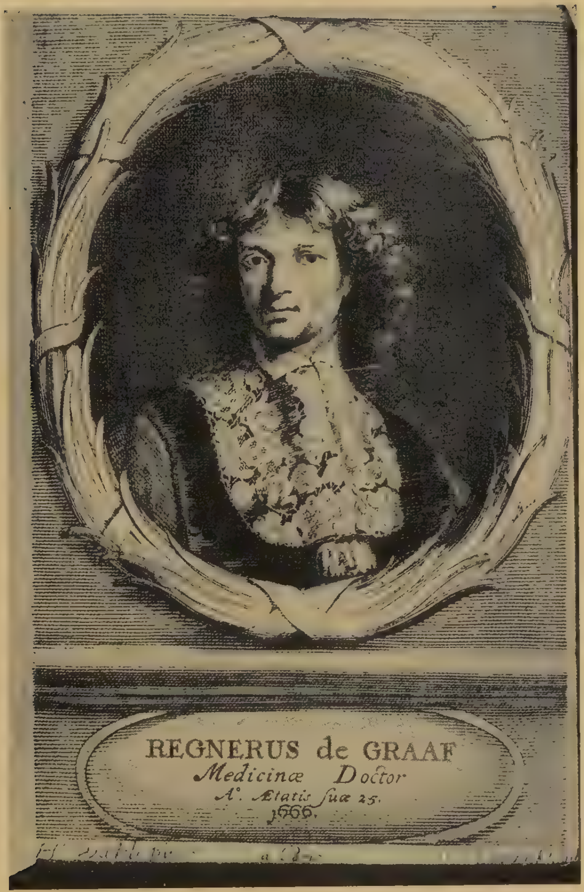

REGNERUS de GRAAF
Medicinæ Doctor
A°. Ætatis suæ 25.
1666.

Figure 29. De Graaf at 25 (from the first edition of his *De virorum organis generationi*, 1668).

De Graaf also studied the reproductive organs both of male and female, and was the first to describe the ovarian follicles which still bear his name.

CHAPTER III

IN WHAT MANNER THE PANCREATICK JUICE WAS FOUND OUT

THE First Experiment by which we undertook to collect the *P*ancreatick juice in a living Dog, was a Ligature with which we tied the upper-part of the Pancreas, together with the thin Gut; for, by this manner, we hoped that after some Hours we should have found the *P*ancreatick Duct swell'd with Juice, but in vain: which seemed to our Judgment to happen by reason that the motion of the Blood being hindered to the *P*ancreas, and separation of the juice from it was prevented also.

The Second Experiment was also by ligature made about the Insertion of the Ductus into the Intestinum Duodenum, but also in vain. The Reason perhaps was the Glandules of the *P*ancreas being hurt, by whose Ductus all the *P*ancreatick Juice might the more easilier [sic] have flown out, by reason that neither in the great Ductus nor in the lateral branches is there any valves found.

The Third Experiment was by two boards or planks, higher in the middle, than at the ends, applyed and straightly bound to the Duodenum, at the ingress of the *P*ancreatick Ductus; from whence, after some hours, the Abdomen being opened again, which before had been tightly stitched up, we found the *P*ancreatick Ductus swelled with a clear and limpid Juice; nevertheless, we could not conveniently either take it out, or taste it. By which success we being animated the more, resolved a fourth Tryal, by opening the Intestinum Duodenum, according to the Longitude thereof; and presently applying a little vessel to the orifice of the Ductus *P*ancreaticus, as the first Figure of the following Table A. [Fig. 30] demonstrates: after wards by straightly tying the said Intestine about the neck of the vessel: so that its orifice was diametrically opposite to the end of the Ductus *P*ancreaticus, not doubting but by this means we should gather a rare quantity of the *P*ancreatick Juice; but this also in vain: without doubt, because the air included within the vessel, denyed

---

translated from the second Latin edition by Christopher Pack, appeared in 1676 under the title *De Succo Pancreatico: or, A physical and anatomical treatise of the nature and office of the Pancreatick Juice.* London.

entrance to the *P*ancreatick Juice, lightly touching it. Therefore we resolved to try a Fifth Experiment, with a little vessel smally perforated, as the first Figure in the Second Table shows under letter *B.* By which advantage, in the space of five hours, we collected so great a quantity of Liquor, that the vessel was almost half full; whose contained Liquor was a bitter relish, and of a yellowish colour; which we judged to happen because the bile, (by reason the Intestine was not first cleaned) was intermixed with the Succus *P*ancreaticus. Wherefore, after many and tiresome vexations of mind, we came to a Sixth Experiment; which seeing it in all respects answered our Expectations: here wee will add its exact description for the sake of the Curious, that they may give credit to their proper senses, which in other words must easily lessen the Credit.

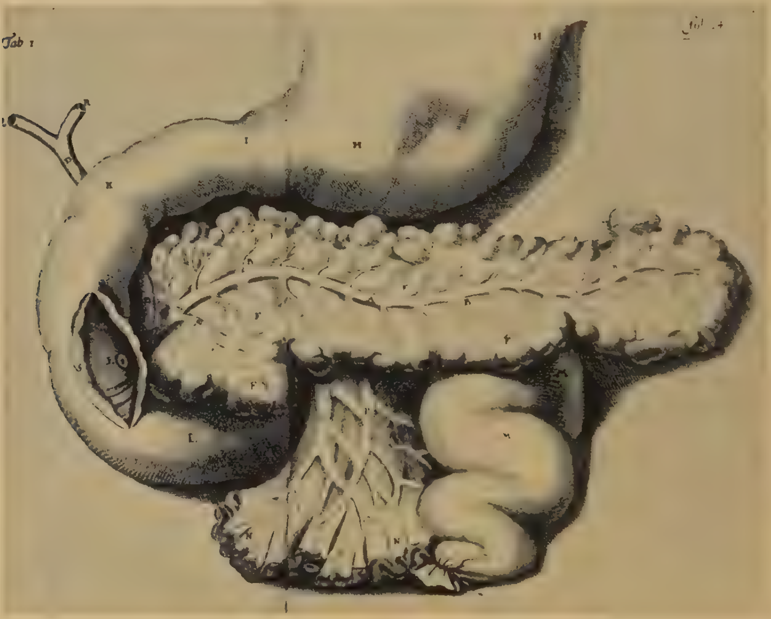


FIGURE 30. De Graaf's engraving of the pancreas and the opening of the pancreatic duct (from the "Succi Pancreatici", 1671).

A little Vessel, with a long neck, was taken, as in the II Table under the letter A. represents; in the upper part of whose Belly a little hole was pierced B.; by which the air included in it, gave way to the Pancreatick Juice.

Let the neck of the Vessel be encompassed with a little cord C.; and severall Rings of Iron, thereunto affixed, or any other convenient thing; by the advantage of which, the Intestine may the more easily be stretched up. Furthermore, you must take a wild Ducks quill D. because that kind of bird hath longer and thinner than all others, which must be so obvolved about the larger part there of with Paper, a little besmeared with boiled Starch, that the orifice of the vessel H. whilst it is included in it, may be most exactly closed: lest either the Bile or Blood, penetrating by the sides of the quill, defile the juice collected, or to be collected in the Vessel.

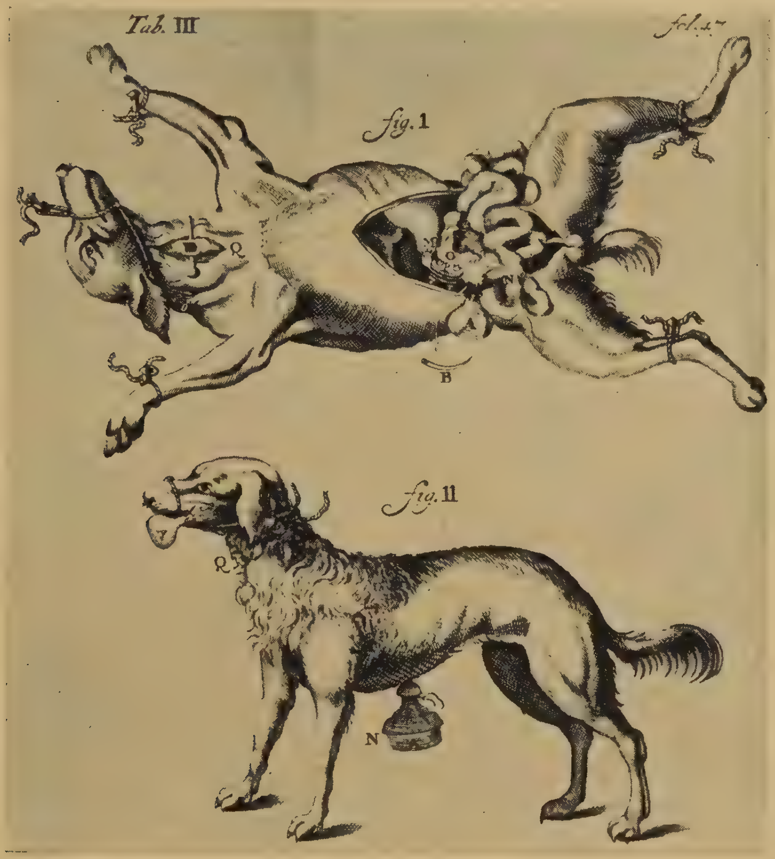


FIGURE 31. De Graaf's illustration of a temporary pancreatic fistula with collecting vessel (from "Succi Pancreatici", 1671).

This quill is affixed to the Vessel, by reason of the straightness of the Pancreatick Duct, which will not admit the neck of the Vessel. Presently you must take a little tap or stopple made of soft wood, and of such thickness that it may fill up the narrower orifice *G.* which with the Allegated thred *K*. by the help of the Style may be so far protruded through the larger quill *F*. that a little thereof may remain in the larger part of the quill *G*. and there may stick so fast, that it may not return of its own accord into the Ductus Pancreaticus; because then the Pituitous or Vermiculous crusted matter, of the Intestines, continually adhering about the end of the Ductus being moved, would easily constrict to be obstructed; which need not be feared, if the stopple remain in the quill.

RENÉ ANTOINE FERCHAULT DE RÉAUMUR

René Antoine Ferchault de Réaumur (1683-1757), the distinguished French scientist, lived in an age when versatility in science was still a possibility. Like Boyle he invented a thermometer, and the scale of temperatures which he introduced still bears his name. He published a great work on insects and made varied contributions to physics and chemistry. By far the most picturesque of his studies relate to his observations on digestion.[5] He had in his possession a pet kite, a bird of prey which is accustomed to ejecting from its stomach unpalatable articles of food. Réaumur took advantage of this unique opportunity and trained his pet to swallow sponges; when they were brought up, soaked with gastric juice, he found that the fluid squeezed from the sponge caused liquifaction of meat. Unfortunately the buzzard died in the course of his observations and he was forced to continue his studies upon less obliging animals such as ducks and chickens.

GASTRIC JUICE OF THE BUZZARD

It will be easily seen that sponge is the most convenient substance to use in these experiments, for birds of prey do not normally eat it and therefore, judging by previous observations, we may conclude that they cannot digest it. I had no doubt as to the success of the experiment which I was about to undertake, and I accordingly put several small pieces of sponge into a tube, without filling it too full; numerous small holes were then made in the tube and it was swallowed by the bird and brought up as usual. Before the pieces of sponge were placed in the tube they weighed only 13 grains, but when I took them out their weight was 63 grains; they therefore absorbed 50 grains of fluid, most of which I was easily able to squeeze out into a vessel prepared for the purpose.

---

[5] de Réamur, R. A. F. "Sur la digestion des oiseaux. Première mémoire. Experiences sur la manière dont se fait la digestion dans les oiseaux qui vivent principalement de grains et d'herbes, et don't l'estomac est un gésier." *Hist. Acad. roy. d. sci.,* 1752, Paris, 1756 pp. 266-307; "Second mémoire. De la manière dont elle se fait dans l'estomac des oiseaux de proie." *Ibid.* 1752, pp. 461-495 (pp. 481-484).

This experiment alone proves that a fairly large quantity of juice can be obtained quite easily. Two or three of these tubes containing sponge, administered in the course of the day would yield double or treble the above amount, *i.e.* 100 or 150 grains of fluid, while for a small outlay two or three birds could be kept for a week or two and thus 200, 300, or even 450 grains of juice obtained daily. A still greater quantity of this fluid might be provided without any expense by those who keep numbers of these birds for the sport at which they excel by their swift flight and great strength. If it were feared that the sharp edges of the tin tube might injure either the bird's stomach, or the passage by which it enters the stomach and is ejected from it,—though it never seemed to do my buzzard any harm,—then let a leaden tube with smooth rounded edges by substituted. Such a tube would be no more harmful than the lead pills given to birds of prey as a medicine, and would, indeed, take their place. If the amount of fluid obtainable from a buzzard, or from any bird of prey of that size, is still insufficient, one could get much larger quantities, which would be enough for a great many experiments, from larger birds such as vultures or eagles. My buzzard died before the series of experiments which I had intended to perform upon it were completed, and I blame my negligence in not replacing it by another buzzard or similar bird of prey. However, I shall make amends for this and try some further experiments which seem to me desirable: I shall now indicate which of these I consider to be the most important, in order to encourage other physicians to attempt them if they have the opportunity.

Before my buzzard died I had only twice obtained, by means of sponges, this juice which can dissolve bones and meat. When I squeezed the fluid out of the sponges into a dish it was quite unlike the clear liquid which is got by different distillations, for it was thick and cloudy and a muddy yellowish white in colour. I am not sure whether its natural colour and transparency had been altered, but further observations will elucidate this point. In the first experiments which I made I did not take the precaution of thoroughly washing the sponges, so that if there were any sediment or other matter in them it would change the consistency of the fluid and make it cloudy.

Apart from anything which the fluid might absorb from the sponges, there may be another reason for its impurity. If, before entering the tube, it came in contact with fragments of meat in the stomach it would not fail to act upon them to a certain extent, and some part of this meat would, when digested and reduced to pulp, almost certainly be mixed with the juice. Therefore, although the juice contained in the sponges could dissolve meat it must not be supposed that it is pure. To obtain fluid which is absolutely pure,—or at least much purer than that which we have just mentioned,—it is only necessary to make sure that the bird swallows the tube containing the sponge on an empty stomach, and that it does not have any food while it retains it. This will not be such a hardship as one might imagine, for nature enables these birds to endure very long fasts; they are not always successful in their search for prey and often go for days without catching, and consequently without eating, anything. While M. le Commandeur Godeheu was at Malta he received a live vulture (which he intended for my laboratory, where it now is) from Tripoli, on which he performed an experiment which proves that such birds do not need daily nourishment: in order to dissect it more easily after death he wished the bird to become very thin and accordingly he gave it no food at all; the bird withstood this severe fast for 17 days.

When I put some of the juice from the buzzard's stomach on my tongue, it tasted salt rather than bitter, although, on the contrary, the bones which had been reduced to a jelly by a similar fluid, and their remains, on which the fluid had acted, had not a salt but a bitter taste.

When blue [litmus?] paper was moistened with the fluid it became red.

One of the first experiments that ought to be tried with this fluid,—both because it would be most interesting and because it would prove that it is this juice which reduces meat and bones to pulp,—would be to make it dissolve meat in a vessel just as it dissolves it in the stomach. Actual digestion of aliments taking place under such abnormal conditions would be a most singular and interesting phenomenon. Although my efforts in this direction were not successful I shall recount them. I only made two attempts and they would need to be repeated with precautions which I did not take; indeed, they would probably have to be made many times before all the necessary measures were discovered.

LAZARO SPALLANZANI

ABBÉ LAZARO SPALLANZANI (1729-1799). The most important contributions to the physiology of digestion after René de Réaumur were those of the gifted Italian investigator, Spallanzani. He studied the action of saliva on foodstuffs, verified Réaumur's observations on the digestive powers of gastric juice, proving, in addition, that it prevented putrefaction, and carried out a large number of daring experiments upon himself, which are well illustrated by the following selection.[6] His experiments on respiration are referred to elsewhere.

LIX.

I must now turn to man to conclude my investigations upon digestion in different animals with membraneous stomachs. It is true that the studies designed for this purpose on numerous animals of this class, especially birds of prey, cats and dogs, whose stomachs are very like ours, lead us to conclude that their digestive functions are the same as our own: this, however, is proof by analogy and is, therefore, only a probability; besides, after having reached certain positive conclusions with regard to animals, I had at least to try and do the same with regard to man. Glancing over the works of doctors, both ancient and modern, I find the commonest object of their study is human digestion, but, if I may be allowed to say so, they have sought to guess the way in which digestion works rather than to discover it. Direct experiments on man are altogether lacking, and all that has been done is limited to more or less doubtful conjectures and hypotheses. If, therefore, I had to have recourse to my own experiments when dealing with animal digestion, how much more necessary was it to do so with regard to human digestion. Thinking over the most important experiments which it would be possible to make on man, it seemed to me that they could be brought under two principal groups, *i.e.* those in which human gastric juice is obtained in order to repeat the experiments made with the same juice in animals, and those in which tubes containing various animal and vegetable substances are swallowed, in order to study the changes which they will have undergone when they emerge from the body. I intended to make these experiments on myself, but I admit that those involving the use of tubes seemed to me rather dangerous, for I knew that bodies held up in the stomach without being digested

---

[8] Spallanzani, L. "Della digestione degli animali" in his *Fisica animale,* Modena, 1780, vol. 1, pp. 1-275. There were many French editions of this work (*e.g.* 1785; also 1893).

had led to dire consequences and, after a considerable time, had been vomited up. I remembered too, cases where similar bodies had been held up in the intestines. However, the various contradictory facts which are current encouraged me to try these experiments; I knew that very hard stones, like those of cherries, morellas, medlars and plums were swallowed with impunity by children and country-people and that they passed through the anus very easily without causing the slightest discomfort: in the midst of this struggle the previous events which I recorded induced me to overcome my reluctance.

LX.

It was a question of swallowing a little linen bag, containing 52 grains of masticated bread. I began this experiment one morning on rising, and while fasting, and the circumstances which I am about to relate apply to all my experiments of this kind. I retained this bag for 23 hours, without experiencing any ill-effects; on emerging it contained no bread, the thread with which the two sides of the bag had been sewn was neither broken nor damaged, the same applied to the thread at the mouth of the bag. The linen was not torn in any way, so that, evidently, it had not undergone any alteration either in the stomach or intestine. The success of this experiment encouraged me to try others; I repeated it with two similar bags, containing an equal amount of masticated bread, but with this difference, one of the bags was made of two thicknesses of linen, the other of three: you may guess, from what I have said elsewhere, that I wanted to find out whether the thickness of the bag would make digestion more difficult. I observed as follows: the two small bags emerged from my body after twenty-seven hours; the bread in the bag made of two thicknesses had been entirely digested, but there was a little left in the one made of three thicknesses; this fragment of bread had lost its taste while retaining its other properties.

LXII.

Having discovered that I could digest meat which had been cooked and masticated, I wanted to find out whether I could digest the same meat unmasticated; I swallowed, therefore, 80 grains of gristly meat from a chicken's breast in a small bag: I ejected it only after 37 hours. It had lost 56 grains and what was left, far from being gelatinous or tender, was dry and the inmost fleshy fibres seemed less dry than those outside. Otherwise, digestion appeared to have taken place equally, as the piece of meat kept the shape into which I had cut it.

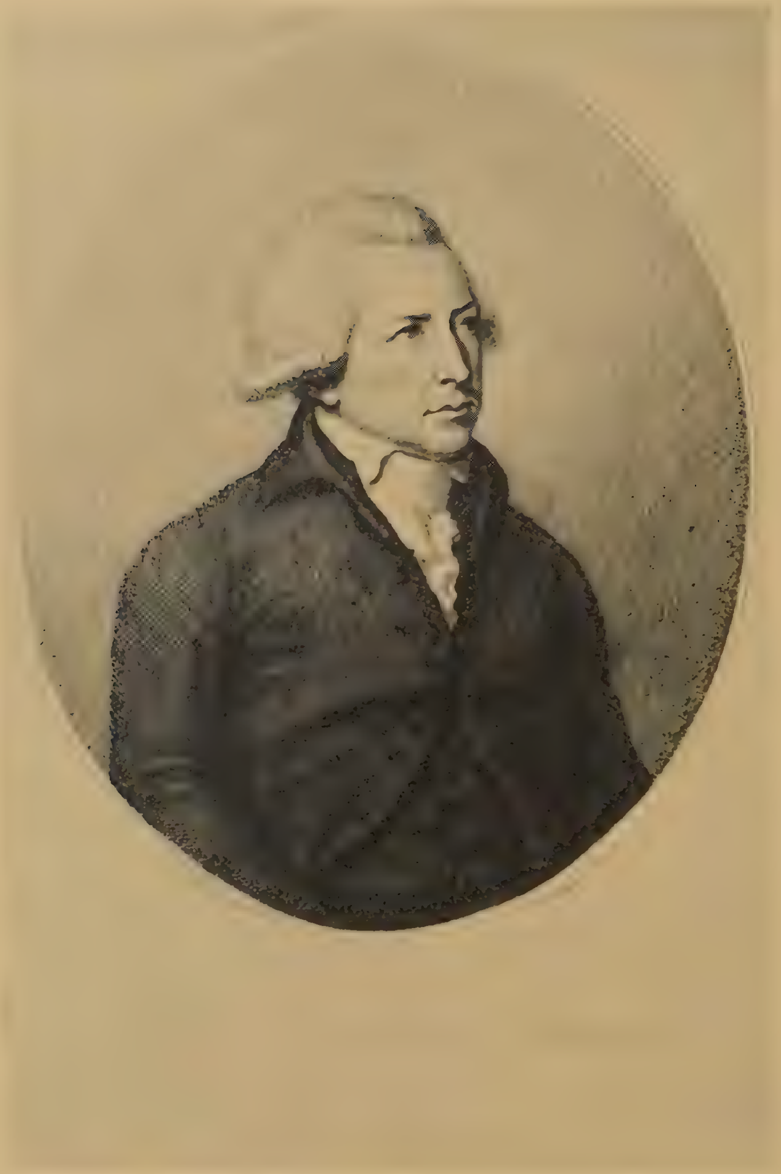
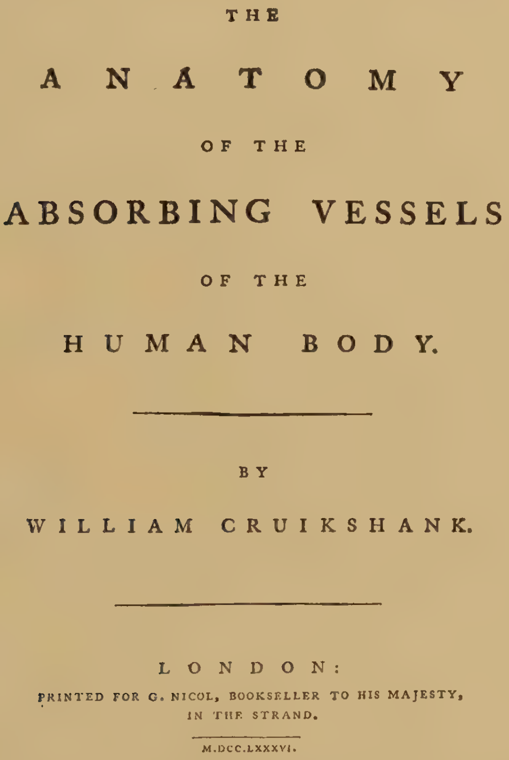


FIGURE 32. Dickinson's engraving of William Cruikshank.

WILLIAM CUMBERLAND CRUIKSHANK

William Cumberland Cruikshank (1745-1800), the personal physician of Dr. Johnson, was a pupil of William Hunter and, in conjunction with the Hunters, John and William, and their lamented collaborator, William Hewson (1739-1774), laid the foundation of modern knowledge concerning the function of the lymphatics. Cruikshank was an exceptionally handsome man who had a large practice as a physician, but he found time to cultivate scholarly tastes and to develop a literary style which received the commendation of his celebrated patient. He had in addition an historical sense, well-illustrated in the first part of the following passage,[7] which was unusual among English medical writers of the 18th century.



THE

ANATOMY

OF THE

ABSORBING VESSELS

OF THE

HUMAN BODY.

BY

WILLIAM CRUIKSHANK.

LONDON:
PRINTED FOR G. NICOL, BOOKSELLER TO HIS MAJESTY,
IN THE STRAND.

M.DCC.LXXXVI.

Figure 33. The title-page of Cruikshank's book on the lymphatics, 1786.

THE HUMAN LACTEALS

Though Asellius had not seen the lacteals in men, he inferred their existence from analogy, and firmly asserted it. But this doctrine was far from being generally received; and the doctrine of Hippocrates and Galen, which taught that the chyle was absorbed from the intestines by the red veins, more generally prevailed; and Asellius's vessels were considered by the greater number of anatomists as fictitious. Nor was this to be wondered at: they were not only influenced from respect to the ancients, but Harvey, the great discoverer of the circulation of the blood, then in his career of glory, opposed the doctrine, and never believed in the existence of Asellius's lacteals.

---

[7] Cruikshank, W. C. *The anatomy of the absorbing vessels of the human body.* London: G. Nicol, viii+192 pp., 3 pl., 1786 (pp. 33, 34, 35, 36, 41-42).

For several years, little was added to Asellius's discovery: but in 1634, Veslingius, according to Haller, first saw the lacteals in men, and gave a figure of them. This figure is not very correct; but neither are the figures of the skeleton itself, given by the earlier anatomists, more correct: nor have we a right to expect, that a person who sees any thing for the first time, can conceive it, or draw it, as well as more opportunities would have enabled him to do, or as one who comes after him, with the advantage of his knowledge, may be able to do. It appears also, from passages alluded to by Haller in Veslingius's posthumous works, that he was the first who saw the lymphatics of the liver, though he took them for lacteals. As Bartholin, to whose care these works were entrusted, must have read these passages, Haller thinks it extremely probable, that it was there he received his first information of the lymphatics.

Whatever Veslingius might have known, it has been latterly understood that Rudbeck, a Swede, twenty-eight years after Asellius's discovery of the lacteals, without any previous information on this subject, also discovered the lymphatics in quadrupeds. He supposed them a fifth set of vessels; and as they neither carried red blood, like arteries and veins, nor chyle, like the lacteals, but a transparent fluid, like serum, he calls them Vasa Serosa.

About the same time, Bartholin, the Dane, also saw these vessels; but, independent of the hints he received from Veslingius, there are suspicions that he must have previously heard of Rudbeck's discovery; for, in his publication on this subject, he says, "Sibi vasorum serosorum nomen non placere quod aliqui his vasis imposuerint."—Bartholin changed the name into Vasa Lymphatica, a name they have since retained; for, as he first published an account of them, and as he was a man of more eminence than Rudbeck, the whole medical world gave him the credit of the discovery. He himself, however, seems to be content to share this discovery with Rudbeck and Jolyffe.

Bartholin having mentioned Dr. Jolyffe, it may be proper also to state his right to the discovery of the lymphatics. Glisson says, that in the beginning of June 1653, Dr. Jolyffe, who was then taking his degree at Cambridge, informed him, "Dari vasorum quartum genus a venis, arteriis, nervisque plane diversum, idemque ad omnes aut plurimas saltem corporis partes distribui, & humorem aquosum in se complecti. Addebat porro se in compluribus animalibus eorundem ductum investigasse in artubus, scil. testiculis, utero, aliisque etiam partibus: certoque sibi constare liquorem in iis intro versus mesenterium tendere, & particulatim ad initium sive redicationem ejus."

Though, in compliance with anatomists in general, I have considered the Absorbent System as consisting of two parts, and have given the history of the discovery of each part; yet, in fact, lacteals and lymphatics are branches of one common trunk; and therefore Veslingius, Rudbeck, Bartholin, and Jolyffe, may be rather said to have seen the vessels first seen by Asellius, in other parts of the body than the intestines, mesentery, and liver. They did not properly discover a new set of vessels, but some more branches of the same system. On the other hand, Asellius had an idea that his vessels were formed only for the purpose of carrying the chyle into the blood; he had no conception of their existing any where else; so that, without the discovery of the lymphatics, we must have remained ignorant of the greatest part of the absorbent system; and therefore they are equally entitled to the honour bestowed on discoverers of so important a part of our machine.

CHAPTER VIII

FURTHER CONFIRMATION OF THE ABSORPTION OF FLUIDS BY THE LYMPHATIC VESSELS

That the lacteals absorb from the intestines, has been so fully proved, that there is not now an anatomist living, who has the smallest doubt concerning the fact. They have not only been seen absorbing the chyle, but they take up, very readily, coloured fluids thrown into the intestines. Every experiment Mr. Hunter made on the intestines of living animals, at the same time that it refuted absorption by red veins, in the strongest manner confirmed absorption by the lacteals. They quickly absorbed the milk, the solution of starch in water, coloured with indigo, the musk-water; in short, every fluid which was thrown into the cavity of the intestines. I have already mentioned the arguments which induced

Dr. Hunter to advance the doctrine, that lacteals and lymphatics were the same species of vessels, and that both absorbed. I come now to offer some additional proofs of this. An accustomed eye finds very little difficulty in distinguishing lymphatics from every other species of vessel, in men or quadrupeds; their valves, their general appearance, their intercourse with conglobate glands, sufficiently mark them. Now the lymphatics are not only branches of the same trunk, as Dr. Hunter observed, but there is such a connection between them, such as anastomosis, that the fluids absorbed by the lacteals are in part transmitted to the lymphatics, and through them, at last, conveyed into the blood. A very remarkable instance of this kind I demonstrated at lecture in Windmill Street, about two years ago. The lymphatics of the diaphragm were seen turgid with chyle, which they had received from the lacteals, some of which were passing that way, towards the subclavian veins. A stronger proof that lymphatics are absorbents, is, that whenever fluids are extravasated on surfaces, or into cavities, or whenever such fluids preternaturally distend their reservoirs, the lymphatics belonging to these surfaces and cavities are found full of the same fluid. This is better demonstrated, when the fluids mentioned happen to be of a strong colour. Thus I have repeatedly seen, in animals dying of hæmoptoe, and in the human subject itself, the lymphatics of the lungs, which at other times contain a transparent fluid, turgid with blood, which they had absorbed from the air-cells. Where gall-stones, in the ductus communis coledochus, or in the cystic duct, have prevented the bile from flowing into the intestines, and the gall-bladder, in consequence of this, became preternaturally distended with that fluid, I have also seen the lymphatics of that reservoir full of the bile they had absorbed from its cavity. Baron Haller asserts, that he had repeatedly seen the lymphatics, as well as the lacteals, full of the coloured fluid he had thrown into the living body. "In animale, cui plena fuerunt aut chylo, aut lympha, aut cæruleo liquore, quem animalia, absorbere coegi, sub ipsis intentis meis oculis, toties vidi haec, sive lymphatica vascula, sive lactea evanescere." Malpighi suspected that the lymphatics persisted in absorbing, even for some time after death; and I found this to be true in quadrupeds: on making ligatures on the trunks of the principal blood vessels, no lymphatics were then visible; but in an hour after I found them turgid with lymph. Mascagni, Professor of Anatomy at Sienna, in his Prodrome to his History of the Lymphatics, asserts, that fluids thrown into cavities, get into the absorbents many hours, or even days, after the body is dead. After what I have said of transudation in dead bodies, it may be doubted whether this penetration of fluid was absorption, or transudation only.

WILLIAM PROUT

William Prout (1785-1850), the first English physiological chemist, is well-known to the historians of pure chemistry for his extraordinary speculation that the atomic weights of all the elements are exact multiples of the atomic weight of hydrogen or half that of hydrogen. Though he had not the facilities at that time to obtain the necessary evidence for his theory, this has stimulated more investigation during the 115 years since it was put forward than any other generalization in the field of chemistry. As a physiological chemist Prout is scarcely less distinguished, and his discovery that the stomach contains free hydrochloric acid will always remain one of the classics of physiological literature. It has the virtue of being brief, clear and final, as the following passage,[8] which includes nearly two-thirds of the original text, well indicates.

ON THE NATURE OF THE ACID AND SALINE MATTERS USUALLY EXISTING IN THE STOMACHS OF ANIMALS

That a free, or at least an unsaturated acid usually exists in the stomachs of animals, and is in some manner connected with the important process of digestion, seems to have been the general opinion of physiologists till the time of SPALLANZANI. This illustrious philosopher concluded, from his numerous experiments, that the gastric fluids, when in a perfectly natural state, are neither acid nor alkaline. Even SPALLANZANI, however, admitted that the contents of the stomach are very generally acid; and this accords not only with my own observations, but with that, I believe, of almost every individual who has made any experiments on the subject.

The contents of the stomach of a rabbit, fed on its natural food, were removed immediately after death, and repeatedly digested in cold distilled water till they ceased to impart anything to that fluid. The whole of these different portions of fluid, which always exhibited strong and decided marks of acidity, were then intimately mixed together, and after being allowed to settle, were divided into four equal portions. 1. The first of these portions was evaporated to dryness in its natural state, and the residuum burnt in a platinum vessel; the saline matter left was then dissolved in distilled water, and the quantity of muriatic acid present determined by nitrate of silver in the usual manner; the proportion of muriatic acid, in union with the fixed alkali, was thus determined. 2. Another portion of the original fluid was super-saturated with potash, then evaporated to dryness, and burnt, and the muriatic acid contained in the saline residuum determined as before. In this manner the total quantity of muriatic acid present in the fluid was ascertained. 3. A third portion was exactly neutralised with a solution of potash of known strength, and the quantity required for that purpose accurately noticed. This gave the proportion of free acid present; and by adding this to the quantity in union with a fixed alkali, as determined above, and subtracting the sum from the total quantity of muriatic acid present, the proportion of acid in union with ammonia, was estimated. But as a check to this result, the third neutralised portion above mentioned was evaporated to dryness, and the muriate of ammonia expelled by heat, and collected. The quantity of muriatic acid this contained was then determined as before, and was always found to represent nearly the quantity of muriate of ammonia as before estimated; thus proving the general accuracy of the whole experiments beyond a doubt. 4. The remaining fourth portion of the original fluid was reserved for miscellaneous experiments, and particularly for the purpose of ascertaining whether it contained any other acid besides the muriatic. The experiments above mentioned seemed to preclude the possibility of the presence of any destructible acid; and the only known fixed acids likely to be present were the sulphuric and phosphoric; the muriate of barytes, however, neither alone, nor with the addition of ammonia, produced any immediate precipitate,[9] showing the absence of these two acids in any sensible quantity, and still farther confirming the results as before obtained.

---

[8] Prout, W. "On the nature of the acid and saline matters usually existing in the stomachs of animals." *Phil. Trans. Roy. Soc.*, vol. 114, pp. 45-49, 1824 (pp. 45-47).

WILLIAM BEAUMONT

William Beaumont (1785-1853), a physician stationed at a military post in the primæval forest of northern Michigan, grasped the unique opportunity of studying the processes of digestion in the victim of a gunshot wound which had caused a permanent gastric fistula. The story of Alexis St. Martin's accident and of Beaumont's wisdom in the management of the case are clearly set forth

[9] It may be proper to remark, that ammonia, after some time, caused a flocculent precipitate, consisting of the earthy phosphates in union with vegetable and animal matter, and that after combustion, traces of sulphuric acid, the result of that process, were very perceptible. But it is evident, from the experiment related in the text, that neither of these acids previously existed in the original fluid in a free state.

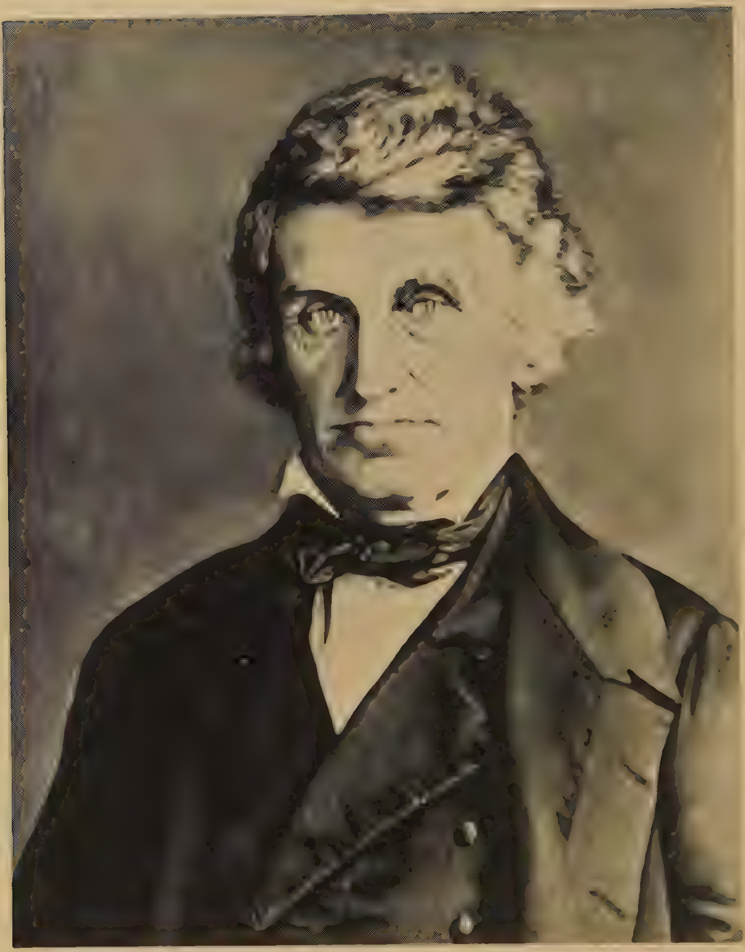


FIGURE 34. William Beaumont at the age of 66 (from an old daguerreotype; obtained through the courtesy of Dr. Samuel Harvey).

in Beaumont's own words which follow. The accident, it will be recalled, occurred on June 6th, 1822. The patient had recovered within a few months, and Beaumont attempted during the next two years, by repeated dressings, to close the wound. The first observations of a physiological nature were commenced in May, 1825, and a preliminary account of them was published in the Philadelphia *Medical Recorder* (vol. 8, p. 14, 1825), in which the observations were erroneously attributed to Surgeon-General Joseph Lovell who had submitted the manuscript to the journal on behalf of Beaumont. Full details of his studies were published in a separate volume in 1833.[10] After giving the case history of Alexis St. Martin, Beaumont described briefly the work of his predecessors in the same field and then put down his epoch-making observations upon movements of the stomach during digestion, the normal appearance of the gastric mucous membrane, the fact that gastric juice is secreted only as a result of the taking of food, mechanical irritation being ineffective. By a series of ingenious arguments he concluded that, in addition to free hydrochloric acid, which Prout had previously observed, there was also present in the gastric juice another active chemical substance, to which Schwann in 1835 gave the name of pepsin. Beaumont's observations illustrate the enormous contribution which may come from painstaking clinical observation and those who read his little book must inevitably feel the inspiration of his great example.

PREFACE

The present age is prolific of works on physiology; therefore in offering to the public another book relative to an important branch of this science, it will perhaps be necessary to assign my motives.

They are, first, a wish to comply with the repeated and urgent solicitations of many medical men who have become partially acquainted with the facts and observations it is my intention to detail; men, in whose judgment I place confidence, and who have expressed their conviction of the deep importance of the experiments, the result of which I mean herewith to submit to the public: secondly, (and it is that which mainly influences me,) my own firm conviction that medical science will be forwarded by the publication. . . . .

The experiments which follow were commenced in 1825, and have been continued, with various interruptions, to the present time, (1833.) The opportunity for making them was afforded to me in the following way.

Whilst stationed at Michillimackinac, Michigan Territory, in 1822, in the military service of the United States, the following case of surgery came under my care and treatment.

---

[10] Beaumont, W. *Experiments and observations on the gastric juice and the physiology of digestion.* Plattsburgh, F. P. Allen, 280 pp., 1833 (p. 5; pp. 9-10; pp. 125-127). A facsimile reproduction with Sir William Osler's essay on Beaumont, was published in 1929 by the Harvard University Press.

Alexis St. Martin, who is the subject of these experiments, was a Canadian, of French descent, at the above mentioned time about eighteen years of age, of good constitution, robust and healthy. He had been engaged in the service of the American Fur Company, as a voyageur, and was accidentally wounded by the discharge of a musket, on the 6th of June, 1822. . . . . The whole mass of materials forced from the musket, together with fragments of clothing and pieces of fractured ribs, were driven into the muscles and cavity of the chest.

I saw him in twenty-five or thirty minutes after the accident occurred, and, on examination, found a portion of the lung, as large as a Turkey's egg, protruding through the external wound, lacerated and burnt; and immediately below this, another protrusion, which, on further examination, proved to be a portion of the stomach, lacerated through all its coats, and pouring out the food he had taken for his breakfast, through an orifice large enough to admit the fore finger.

[He then tells the details of his stormy convalescence and gradual recovery with the formation of a gastric fistula through which all his food passed when his side was not tightly bandaged.]

EXPERIMENT I

August 1, 1825. At 12 o'clock M., I introduced through the perforation, into the stomach, the following articles of diet, suspended by a silk string, and fastened at proper distances, so as to pass in without pain—viz.:—a piece of high seasoned *a la mode beef;* a piece of *raw, salted, fat pork;* a piece of *raw, salted, lean beef;* a piece of *boiled, salted beef;* a piece of *stale bread;* and a bunch of *raw, sliced cabbage;* each piece weighing about two drachms; the lad continuing his usual employment about the house.

At 1 o'clock P.M., withdrew and examined them—found the *cabbage* and bread about half digested: the pieces of *meat* unchanged. Returned them into the stomach.

At 2 o'clock, P.M., withdrew them again—found the *cabbage, bread, pork,* and *boiled beef,* all cleanly digested, and gone from the string; the other pieces of meat but very little affected. Returned them into the stomach again.

At 2 o'clock P.M., examined again—found the *a la mode beef* partly digested: the *raw beef* was slightly macerated on the surface, but its general texture was firm and entire. The smell and tast of the fluids of the stomach were slightly rancid; and the boy complained of some pain and uneasiness at the breast. Returned them again.

The lad complaining of considerable distress and uneasiness at the stomach, general debility and lassitude, with some pain in his head, I withdrew the string, and found the remaining portions of aliment nearly in the same condition as when last examined; the fluid more rancid and sharp. The boy still complaining, I did not return them any more.

August 2. The distress at the stomach and pain in the head continuing, accompanied with costiveness, a depressed pulse, dry skin, coated tongue, and numerous white spots, or pustules, resembling coagulated lymph, spread over the inner surface of the stomach, I thought it advisable to give medicine; and, accordingly, dropped into the stomach, through the aperture, half a dozen *calomel pills,* four or five grains each; which, in about three hours, had a thorough cathartic effect, and removed all the foregoing symptoms, and the diseased appearance of the inner coat of the stomach. The effect of the medicine was the same as when administered in the usual way, by the mouth and oesophagus, except the nausea commonly occasioned by swallowing pills.

This experiment cannot be considered a fair test of the powers of the gastric juice. The cabbage, one of the articles which was, in this instance, most speedily dissolved, was cut into small, fibrous pieces, very thin, and necessarily exposed, on all its surfaces, to the action of the gastric juice. The stale bread was porous, and, of course, admitted the juice into all its interstices; and probably fell from the string as soon as softened, and before it was completely dissolved. These circumstances will account for the more rapid disappearance of these substances, than of the pieces of meat, which were in entire solid pieces when put in. To account for the disappearance of the fat pork, it is only necessary to remark, that the fat of meat is always resolved into oil, by the warmth of the stomach, before it is digested. I have generally observed that when he has fed on fat meat or butter, the whole superior portion of the contents of the stomach, if examined a short time after eating, will be found covered with an oily pellicle. This fact may account for the disappearance of the pork from the string. I think, upon the whole, and subsequent experiments have confirmed the opinion, that fat meats are less easily digested than lean, when both have received the same advantages of comminution. Generally speaking, the looser the texture, and the more tender the fibre, of animal food, the easier it is of digestion.

This experiment is important, in a pathological point of view. It confirms the opinion, that undigested portions of food in the stomach produce all the phenomena of fever; and is calculated to warn us of the danger of all excesses, where that organ is concerned. It also admonishes us of the necessity of a perfect comminution of the articles of diet.

IVAN PETROVITCH PAVLOV

Ivan Petrovitch Pavlov, the distinguished physiologist of Russia, who can lay claim to the creation of two special and particularly fruitful fields of physiological thought, was the son of a Russian priest of the Ryazan Government. He was a pupil of Heidenhain and Ludwig, and derived great inspiration from their teachings. It is interesting to note that he did not "find" himself until he had passed his fortieth year when he began his investigations upon the physiology of the stomach. His teacher Heidenhain had made artificial fistulae in the dog, but in making the operation the nerve supply of the stomach had been largely impaired. Pavlov, by virtue of his ambidexterity and extraordinary operative skill, succeeded in making a miniature stomach as a special pouch attached to the main stomach, both retaining their nerve supply. The miniature stomach opened to the outside of the body and when food was received into the main stomach the miniature pouch secreted gastric juice of the same quality as that secreted to deal with the food. By this means he succeeded for the first time in obtaining samples of gastric juice uncontaminated with food. The following selection contains Pavlov's own description of his operation.[11]

THE STOMACH POUCH

With this in view we (myself and Dr. Khizhin) have modified Heidenhain's operation in the following way. The first incision, which begins in the fundus of the stomach, two centimetres from its junction with the pyloric portion, is carried in the longitudinal direction for ten to twelve centimetres, almost parallel to the long axis of the viscus, and divides both the anterior and posterior walls. A triangular flap is thus formed, the apex of which lies in the great curvature of the stomach. A second incision is made from the inside exactly at the base of this

---

[11] Pavlov, I. P. *The work of the digestive glands.* London, Charles Griffin and Co., Ltd., xiv+266 pp., 2nd ed. 1910 (pp. 13-14). Translated by W. H. Thompson.

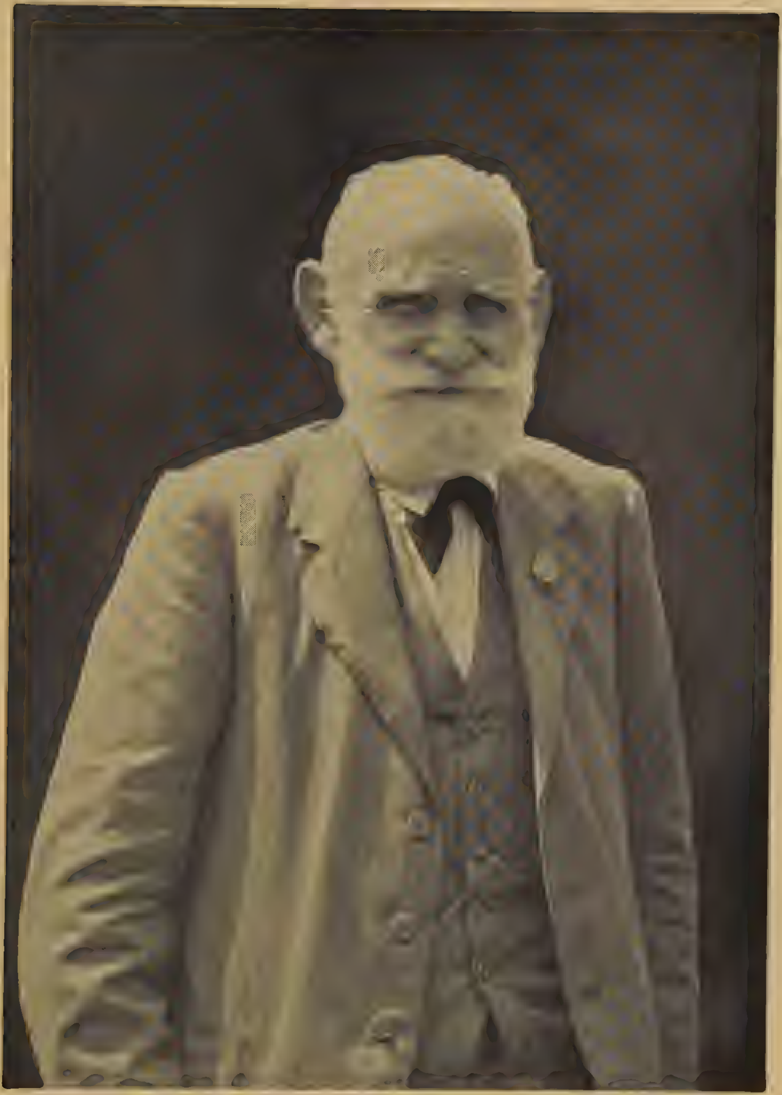


FIGURE 35. A photograph of Pavlov taken at the XIIIth International Physiological Congress, just before his 80th birthday.

flap, but only through the mucous membrane, the muscular and peritoneal coats remaining intact. Thus the serous and muscular coats, and consequently the branches of the vagus nerve, pass uninjured from the wall of the main stomach into the flap of which the main pouch is to be formed. The technical points to be observed in the operation are as follows: The incision in the *linea alba* reaches from the ensiform cartilage downwards for 7-9 cm. Before opening the stomach the cavity is closed off at either end by bands of sterilised india-rubber tubing, tied tightly round the organ. The first incision at the outset is carried only through serous and muscular coats. It is important that its two limbs—one on the anterior, the other on the posterior wall—should be symmetrical to the attachment of the great omentum, otherwise a good pouch cannot be formed. At the bottom of the incision is seen the outside of the mucous membrane, with the blood-vessels running transversely in the submucosa. These are to be double-ligatured and divided, to avoid subsequent bleeding. At first only a minute aperture is to be made in the mucous membrane to allow of disinfection of the interior, which is best done by injecting sterilised 0.5 per cent. hydrochloric acid. When thoroughly cleansed the mucous membrane is divided along both sides of the flap. An apparently difficult part of the operation, the division of the mucous membrane at the base of the flap, is in reality easily carried out. In the first place, with quick light strokes of a sharp knife a superficial incision is made across the whole base of the flap. While making this the assistant precedes the operator, lifting up the mucous membrane with a pair of forceps on either side and holding it tense. A gauze tampon is now laid along the track for two to three minutes, to arrest bleeding. Then the operator goes over the incision with the knife once more, dividing the submucosa down to the muscular coat. In doing this the assistant keeps the tissue tense as before, by holding the edges of the wound apart with the forceps. By this latter procedure a sufficient margin of mucous membrane is freed on either side of the line of incision to allow both flaps to be formed into cup-shaped depressions, and applied back to back, so as to make a double septum of mucous membrane which separates the cavity of the pouch from that of the main stomach. When the submucosa is divided as described, a gauze tampon is once more laid along the incision to arrest bleeding, and, after a little, raised gradually to allow the larger bleeding vessels to be ligatured. To convert the flaps of mucous membrane into dome-shaped recesses, sutures are inserted, as shown in the illustration. These must never pierce the mucous membrane. On the one side they pass through the margin of serous and muscular coats, on the other through submucous tissue only. It is desirable to mark the apex and middle of the base of the flap on either side by a Péan's forceps. Beginning at both bases, the mucous membrane is then united along each margin by four or five sutures to its own adjacent piece of muscular coat. After this the incision in the stomach wall is closed in its whole extent, along both large and small cavities, by a line of Lembert sutures. The orifice of the pouch is to be reduced to the diameter of an ordinary lead pencil, otherwise prolapse of the mucous membrane inevitably occurs. After some practice the whole can be completed in one and a half to two hours.

WALTER BRADFORD CANNON

Walter Bradford Cannon, the successor of Henry Pickering Bowditch as Professor of Physiology at the Harvard Medical School, while still a medical student realized, soon after Röntgen rays had been discovered, that they could be used for the study of gastro-intestinal movements. He found that bismuth, which is opaque to x-rays, served admirably to bring out the contour of the stomach and intestines during activity, and in so doing he introduced a clinical method of diagnosis which since 1898 has been widely used in every hospital of the world, and also a method for study of normal intestinal movements in the intact animal. The diagnosis of gastric ulcer and malignancy of any part of the gastro-intestinal tract by means of the bismuth meal and fluoroscope is now an everyday occurrence, and it is often forgotten that the original contribution came from the physiological laboratory. The following passage is taken from Cannon's description of his first experiments.[12]

THE MOVEMENTS OF THE STOMACH STUDIED BY MEANS OF THE RÖNTGEN RAYS[13]

Since the stomach gives no obvious external sign of its workings, investigators of gastric movements have hitherto been obliged to confine their studies to pathological subjects or to animals subjected to serious operative interference. Observations made under these necessarily abnormal conditions have yielded a literature[14] which is full of conflicting statements and uncertain results. The only sure conclusion to be drawn from this material is that when the stomach receives food, obscure peristaltic contractions are set going, which in some way churn the food to a liquid chyme and force it into the intestines. How imperfectly this describes the real workings of the stomach will appear from the following account of the actions of the organ studied by a new method. The mixing of a small quantity of subnitrate of bismuth with the food allows not only the contractions of the gastric wall, but also the movements of the gastric contents to be seen with the Röntgen rays in the uninjured animal during normal digestion. An unsuspected nicety of mechanical action and a surprising sensitiveness to nervous conditions have thereby been disclosed.

---

[12] Cannon, W. B. "The movements of the stomach studied by means of the Roentgen rays." *Amer. Jour. Physiol.*, vol. 1, pp. 359-382, 1898 (pp. 359, 367, 370-372).

[13] The first account of this work was given at the meeting of the American Physiological Society, in May, 1897 (see Science, June 11, 1897); and the later results were presented at the meeting of the Society in December, 1897. A summary of the results was published in the Proceedings of the American Physiological Society, this Journal, 1898, i, p. xiii. A report of the research was also made to the Boston Society of Medical Sciences, February 15, 1898.

Within five minutes after a cat has finished a meal of bread, there is visible near the duodenal end of the antrum a slight annular contraction which moves peristaltically to the pylorus: this is followed by several waves recurring at regular intervals. Two or three minutes after the first movement is seen, very slight constrictions appear near the middle of the stomach, and, pressing deeper into the greater curvature, course slowly towards the pyloric end. As new regions enter into constriction, the fibres just previously contracted become relaxed, so that there is a true moving wave, with a trough between two crests. When a wave swings round the bend in the pyloric part the indentation made by it deepens; and as digestion goes on, the antrum elongates and the constrictions running over it grow stronger, but, until the stomach is nearly empty, they do not entirely divide the cavity. After the antrum has lengthened, a wave takes about thirty-six seconds to move from the middle of the stomach to the pylorus. At all periods of digestion the waves recur at intervals of almost exactly ten seconds. So regular is this rhythm that many times I have been able to determine within two or three seconds when a minute had elapsed simply by counting six similar phases of the undulations as they passed a given point. It results from this rhythm that when one wave is just beginning, several others are already running in order before it. Between the rings of constriction the stomach is bulged out, as shown in the various outlines in Figures 3, 4, and 5. The number of waves during a single period of digestion is larger than might possibly at first be supposed. In a cat that finished eating fifteen grams of bread at 10.52 A.M., the waves were running regularly at 11:00 o'clock. The stomach was not free from food until 6.12 P.M. During that time the cat was fastened to the holder at intervals of half an hour and the waves were always observed, following one another in slow and monotonous succession. At the rate of three hundred and sixty an hour, approximately two thousand six hundred waves passed over the antrum during that single digestive period. . .

---

[14] Poensgen (Die motorische Verrichtungen des menschlichen Magens und ihre Störungen, Strassburg, 1882), gives a comprehensive review of the literature to that date.

The part played by the fundus apparently has not hitherto been properly appreciated. It has been regarded as the place for peptic digestion or as a passive reservoir for food; but it is in fact a most interestingly active reservoir.

The action of the cardiac portion will be best understood by comparing the appearances the stomach presents at various stages in a digestive period. In order to show these stages I carefully made a set of three tracings of the outlines of the stomach as soon as possible after a cat had finished eating, and another set of three every half hour thereafter, until the contents had disappeared (Fig. 36). These tracings were made by placing white tissue paper over the fluorescent screen, and drawing with a thick lead pencil, easily seen, as much of the boundary of the stomach as I could at the end of each expiration. Between the times for making the drawings the cat was allowed to rest quietly on a mat, but care was taken to lay her in the same position on the holder for each drawing. The drawings of each set were afterwards fastened over one another, so that the lines coincided as closely as possible. Another piece of tissue paper was then put over these, and all four sheets were laid on an illuminated pane of glass. It was thus easy to get a composite tracing, which, considering the movement imparted to the stomach by respiration, and the dimness of the shadows in the later stages of digestion, probably represents more exactly than any single drawing the outline of the stomach for each successive period.

A comparison of these drawings shows that as digestion proceeds the antrum appears gradually to elongate and acquire a greater capacity, and that the constrictions make deeper indentations in it. But when the fundus has lost most of its contents, the longitudinal and circular fibres of the antrum contract to make it again shorter and smaller. Its change of form, however, compared with the rest of the stomach, is slight.

The first region to decrease markedly in size is the preantral part of the pyloric portion. The peristaltic undulations, caused by the circular fibres, start at the beginning of this portion, and gradually, by their rhythmic recurrence, press some of the contents into the antrum. As the process continues, the smooth muscle fibres with their remarkable tonicity contract closely about the food that remains, so that the middle region comes to have the shape of a tube (Fig. 36b—1.30 P.M. to 2.30 P.M.), with the rounded fundus at one end and the active antrum at the other. Along the tube very shallow constrictions may be seen following one another to the pylorus.

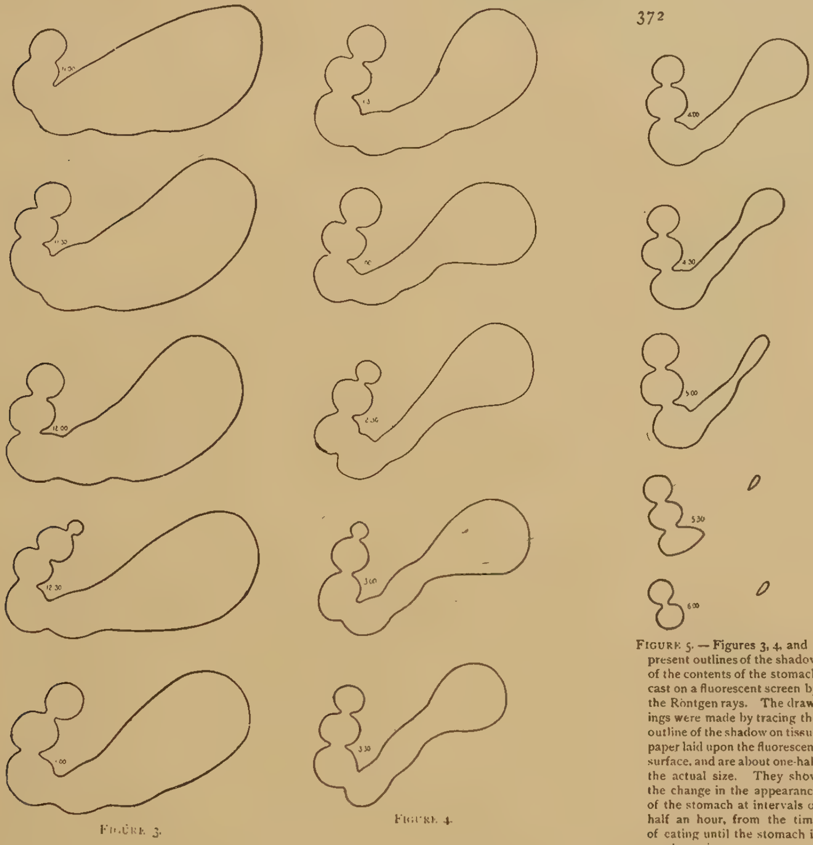


FIGURE 3.

FIGURE 4.

FIGURE 5. — Figures 3, 4, and 5 present outlines of the shadow of the contents of the stomach cast on a fluorescent screen by the Röntgen rays. The drawings were made by tracing the outline of the shadow on tissue paper laid upon the fluorescent surface, and are about one-half the actual size. They show the change in the appearance of the stomach at intervals of half an hour, from the time of eating until the stomach is nearly empty.

FIGURE 36. Cannon's original tracings of the outlines of a cat's stomach at successive intervals following a bismuth meal (*Amer. Jour. Physiol.*, vol. 1, 1898, pp. 369-372).

At this juncture the longitudinal fibres which cover the fundus like radiating fingers, and the circular and oblique fibres reaching in all directions about this spherical region, begin to contract. Thus the contents of the fundus are squeezed into the tubular portion. This process, accompanied by a slight shortening of the tube, goes on until the shadow cast by the fundus is almost wholly obliterated (Fig. 36c—5.30 P.M.).

The waves of constriction moving along the tubular portion press the food onward as fast as they receive it from the contracting fundus; and when the fundus is at last emptied they sweep the contents of the tube into the antrum (Fig. 36c—5.00 P.M. to 6.00 P.M.). Here the operation is continued by the deeper constrictions till finally (in this instance, at 6.12 P.M.) with the exception of a slight trace of food in the fundus, nothing is to be seen in the stomach at all.

WILLIAM MADDOCK BAYLISS AND ERNEST STARLING

Sir William Maddock Bayliss (1866-1924) and Ernest Starling (1866-1927), both professors at University College, London, greatly enriched modern physiology through their prolonged and fruitful collaboration. Their discovery of secretin was peculiarly dramatic, and the simplicity and directness of their original description[15] has an appeal felt even by the uninitiated.

IV. THE CRUCIAL EXPERIMENT

On January 16th, 1902, a bitch of about 6 kilos weight, which had been fed about 18 hours previously, was given a hypodermic injection of morphia some 3 hours before the experiment, and during the experiment itself received A.C.E. in addition. The nervous masses around the superior mesenteric artery and coeliac axis were completely removed and both vagi cut. A loop of jejunum was tied at both ends and the mesenteric nerves supplying it were carefully dissected out and divided, so that the piece of intestine was connected to the body of the animal merely by its arteries and veins. A cannula was inserted in the large pancreatic duct and the drops of secretion recorded. The blood-pressure in the carotid was also recorded in the usual way. The animal was in the warm saline bath and under artificial respiration.

The introduction of 20 c.c. of 0.4% HCl into the duodenum produced a well-marked secretion of 1 drop every 20 secs. lasting for some 6 minutes; this result merely confirms previous work.

But, and this is the important point of the experiment, and the turning-point of the whole research, the introduction of 10 c.c. of the same acid into the enervated loop of jejunum produced a similar and equally well-marked effect.

---

[15] Bayliss, W. M. and E. H. Starling. "The mechanism of pancreatic secretion." *Jour. Physiol.*, vol. 28, pp. 325-353, 1902 (330-332).

Now, since this part of the intestine was completely cut off from nervous connection with the pancreas, the conclusion was inevitable that the effect was produced by some chemical substance finding its way into the veins of the loop of jejunum in question and being carried in the blood-stream to the pancreatic cells. Wertheimer and Lepage have shown,[16] however, the acid introduction into the circulation has no effect on the pancreatic secretion, so that the body of which we were in search could not be the acid itself. But there is, between the lumen of the gut and the absorbent vessels, a layer of epithelium, whose cells are as we know endowed with numerous important functions. It seemed therefore possible that the action of acid on these cells would produce a body capable of exciting the pancreas to activity. The next step in our experiment was plain, viz. to cut out the loop of jejunum, scrape off the mucous membrane, rub it up with sand and 0.4% HCl in a mortar, filter through cotton-wool to get rid of lumps and sand, and inject the extract into a vein. The result is shown in Fig. 37. The first effect

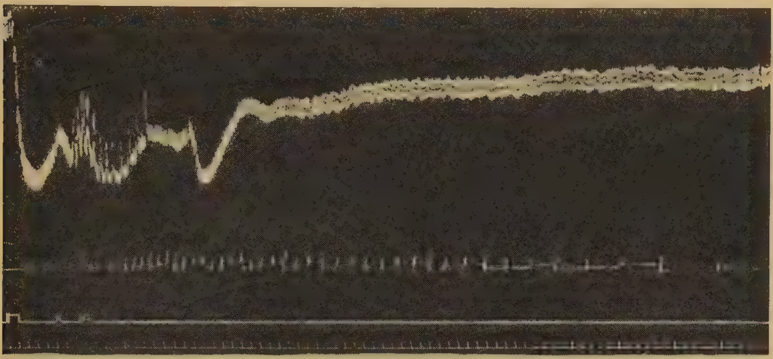


Fig. 2. *Effect of injecting acid extract of jejunal mucous membrane into vein.* Explanation as Fig. 1. The steps on the drop-tracing are due to a gradual accumulation of secretion on the lever of the drop-recorder, which fluid falls off at intervals. Blood-pressure zero = level of drop recorder.

FIGURE 37. Bayliss and Starling's original figure showing the effect on pancreatic secretion and blood-pressure of the intravenous injection of an acid extract of jejunal mucous membrane (*Jour. Physiol.*, vol. 28, 1902, p. 331).

[16] *Journal de Physiologie,* III, p. 695, 1901.

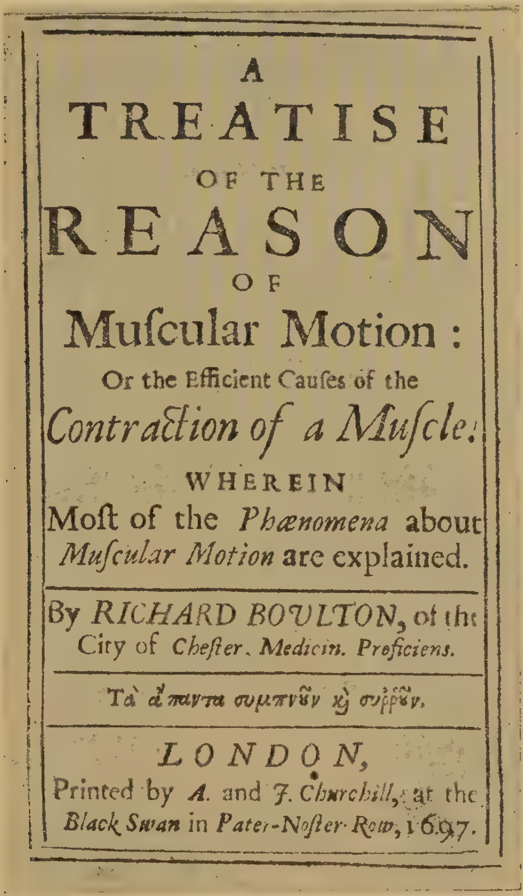
is a considerable fall of blood-pressure, due, as we shall show later, to a body distinct from that acting on the pancreas, and, after a latent period of about 70 secs. a flow of pancreatic juice at more than twice the rate produced at the beginning of the experiment by introduction of acid into the duodenum. We have already suggested the name "secretin" for this body, and as it has been accepted and made use of by subsequent workers it is as well to adhere to it.

In the same experiment we were able to make two further steps in the elucidation of the subject. In the first place the acid extract was boiled and found undiminished in activity, secretin is therefore not of the nature of an enzyme. In the second place, since Wertheimer and Lepage have shown that the effect of acid in the small intestine diminishes in proportion as the place where it is introduced approaches the lower end, so that from the last 6 inches or so of the ileum no secretion of the pancreas is excited, it was of interest to see whether the distribution of the substance from which secretin is split by acids is similar in extent. Fig. 3 shows the result of injecting an extract from the lower 6 inches of the ileum made in the same way as the jejunum extract. The fall of blood-pressure is present, but there is no effect on the pancreas. Another preparation from the ileum just above this one also had no effect on the pancreas. A preparation from the jejunum below the previous one had a marked effect, but less than that of the loop above. The distribution of "prosecretin," as we have proposed to call the mother-substance, corresponds therefore precisely with the region from which acid introduced into the lumen excites secretion from the pancreas.

CHAPTER VI

MUSCLE AND PERIPHERAL NERVES

THE functional activity of muscle was one of the earliest branches of physiology to be investigated. The ancients, especially Aristotle, took shortening for granted and considered the geometrical relations of muscles to joints. Galen gave expression to the theories then current



A
TREATISE
OF THE
REASON
OF
Muſcular Motion:
Or the Efficient Cauſes of the
Contraction of a Muſcle:
WHEREIN
Moſt of the *Phænomena* about
Muſcular Motion are explained.

By *RICHARD BOULTON*, of the
City of *Cheſter. Medicin. Proficiens.*

Τὰ ἅπαντα συμπνοῦν καὶ σύῤῥουν.

LONDON,
Printed by *A.* and *J. Churchill*, at the
Black Swan in *Pater-Noſter-Row*, 1697.

FIGURE 38. The title-page of one of the numerous 17th century tracts dealing with the physiology of muscle. Boulton's work was a small octavo of 116 pages and it contains an excellent summary of knowledge then existing.

concerning the passage along the nerves of "animal spirits" which were believed to cause contraction. In the middle ages and in the 17th and 18th centuries the theory of animal spirits formed the basis of all experimentation and no less a person than Haller was led to believe in the hypothesis, though he defined carefully its limitations. William Croone, who founded the Croonian Lectures, dealt at length with the theory of animal spirits, as did Boulton (see fig. 38), his near contemporary, and the first Croonian Lecturer, Alexander Stuart, fancied that in introducing a blunt probe into the spinal canal he was forcing fluids into the nerves, and that this was responsible for the vigorous contraction caused by such a manipulation. Swammerdam and Glisson had pointed out that muscles when thrown into activity do not increase in bulk, as the notion of animal spirits would seem to demand, but no one heeded their experiments. The developments incident to the discovery of animal electricity by Galvani did not in themselves abolish the theory of animal spirits, but with Helmholtz and the laws of thermodynamics the belief came gradually to be forgotten and the modern conception of polarized membranes was substituted in its place. In recent years the most important advance in the theories of muscular action has been the enunciation of the all-or-none principle. This has defined the type of physico-chemical activity with which one is dealing and it has the additional advantage of emphasizing, as did Nicholas Steno in the 17th century, that to understand muscle we must consider in detail the functional activity of its individual constituents.

GALEN

GALEN (131-201 A.D.), who is mentioned elsewhere (Chapter II), made many interesting observations upon the physiology of muscle and nerve. His experiments on the spinal cord suggest at times that he appreciated the significance of reflex action. However, he put forward the theory that the nervous system controlled muscle through the passage of fluid ("animal spirits") down the nerve trunks and the conception dominated thought in this field until 1792. Much more significant were Galen's simple observations concerning the action of individual muscles and muscle groups. He objected to the theory, apparently prevalent at this time, that there existed more than one type of contractile activity. The following passage[1] from his little book, *De motu musculorum,* illustrates his beliefs concerning contraction and contains, incidentally, some of his observations upon reciprocal innervation. It illustrates also his obscure and redundant style.

---

[1] Galen. *De motu musculorum.* Bk. 1, Chapter 4. The first printed edition of this work, edited and translated from the Greek by Thomas Linacre, appeared in London in 1522 from the press of Pynson. The first French translation was published by Étienne Dolet in 1541. See also Charles Daremberg's *Œuvres anatomiques, physiologiques et médicales de Galien.* Paris: J. B. Baillière, tom. 2, pp. 321-375. Further details concerning

---

Each muscle has only one active movement (that of contraction, since muscles are only extended in passive obedience to the active movement of the opposing muscle) not six, as was commonly believed. Proof of this statement by reason and experiment.

The primary object of our investigation is to discover whether there are as many muscle movements as there appear to be either after vivisection or before dissection, or if there are many more kinds of movement than it would appear. It seems absurd, apart from any other reason, that there should be more than one kind of muscle movement (see infra chap. v and vi), just as it would seem absurd to say that every artery has a different motion, for indeed, nature always appears to act in the same way in organs which are alike. The theory, which has already been advanced, that each muscle has six movements, is obviously fallacious. In reality no muscle in the arms or legs has a third movement apart from extension and contraction. The same is obviously true of temporal muscles, each of which has two movements. If the whole limb is moved by its muscles in six places, there is yet no reason to doubt that each muscle has a double movement. Actually if one muscle had to move the whole limb it would need to be capable of as many movements as the limb has movements; but since there are many more than six muscles in every limb, it is not surprising that the various movements should be performed for the limb by different muscles. I think that those who express such opinions have been deceived by the tongue, which they believed to consist of a single muscle. If this were really the case it would clearly prove that one muscle is capable of many different movements. Since the tongue is not really a single muscle; but is moved by a number of muscles, I think one may conclude, on the contrary, that each muscle is incapable of diverse movements; if it were otherwise the existence of a great number of muscles would be unnecessary, because one alone could perform them all. But, it is said the eyes perform four distinct movements; that is true, my friends, for they have, in fact, four different muscles each, but there would only be one for each eye if it were capable of performing all these four movements. As one would conclude that this

---

the book are given by the editor in *Muscular contraction and the reflex control of movement.* Baltimore: The Williams and Wilkins Co., pp. 8-10, 1926.

muscle had four movements if it were the only one, so, since there are as many muscles as there are movements one is led to believe that each muscle performs one movement; just as one movement only is performed by each of the two rotator muscles of the eye.

But, some of us say, it is admitted that each muscle performs two movements, if not more. How, then, can reason mean that there is only one muscle movement? [In reply I say] there is nothing absurd in that. Each muscle has only one active movement, it is only capable of the opposing movement by accident. A muscle is active when it pulls the limb which is in motion towards it, and not when it is brought back again by an opposing muscle. This is the reason why every limb which can move has more than one muscle. For every muscle situated up above there is also one situated down below; and if there is a muscle on the right there is one on the left too; for, since each limb, set in motion by muscles—as though by reins—has to divide its activity between two sides, has one muscle tense and one relaxed alternately. The contracted muscle pulls towards itself, while the relaxed muscle is pulled along with its part; therefore both muscles move during the performance of each of the two movements, [but they are not both active] for activity consists in tension of the part which moves, and not in the action of obeying; and a muscle obeys when it is pulled in a passive state, just like any other part of the limb.

Dare we then now assert that only one innate movement exists in each muscle or must we first find out whether the various peculiarities of muscle fit in with this view. The latter course seems to me more preferable. Let us then at once state the peculiarities which can be observed in muscle, omitting nothing. There is one peculiarity, the first which we mentioned in the beginning (Chap. I) and that is that if whole muscles are cut through, their lower portion is completely deprived of movement, while if they are partially cut, movement is only injured. The gravity of the injury is in proportion to the incision; the larger the incision the greater the injury and vice versa. Supposing that these same observations are applied to tendons also; indeed if you cut a tendon through you deprive it of movement; if you make an incision the injury is in proportion to it. If then when a single muscle is cut through all movement is destroyed one may conclude, I think, that this one muscle was the source of all movement [in that limb]. If, on the other hand, when a single muscle is cut only one movement was done away with, one might then conclude that the cut muscle was the source of one movement only.

As it happens that not one movement alone, nor yet all movement, but invariably two movements are done away with, it would seem to follow that two movements are performed by one single muscle. At the same time, since incision of a muscle or a tendon situated on opposite sides destroys the same two movements, we may conclude, by an absolutely identical method of reasoning that this muscle or tendon is possibly the source of the same two movements, which it governs or performs equally; so that the loss of any muscle entails the destruction of [active] movement in the opposing muscle, and they cannot both be equally capable of actively producing two opposing movements; each one of them can only perform one of the two movements. One of these propositions is necessarily true; we shall try and discover which, after explaining more clearly, in the first place, that in these successive movements, when one is destroyed the other must necessarily perish also. Suppose that the movement which extends a limb is destroyed, it will be possible to flex the limb again once, but, after that, it will remain in that position and can never extend again because it has been deprived of its extensor movement; being therefore incapable of extension it cannot, in consequence, flex either. In the same way if a limb is deprived of its flexor movement, it is possible to extend it once more, but after that the limb will be immovable since it can never return to the flexed position which must precede extension. It seems, therefore, indisputable that successive opposing movements are simultaneously destroyed, and it is in consequence reasonable to try and discover whether the two movements are produced by both muscles, or whether one movement being produced by each one of them, the second is abolished immediately after the first.

WILLIAM CROONE

William Croone (1633-1684), founder of the Croonian Lectureship, is one of the picturesque figures among the physiologists of the 17th century, and there is no better way of describing the state of knowledge concerning muscle physiology, at that time than by citation from his writings. It will be recalled that he was one of the original founders of the Royal Society of London, which had been officially incorporated in 1662, and on May 4th, 1664, he presented the Society[2] with a copy of his "little treatise" *De ratione motus musculorum* which had appeared anonymously in London in that year.[3] In this work he argued that muscular contraction was brought about through the action of a "spirituous liquor" which passed from the nerves and interacted with substances in the muscle. He despaired of ever knowing how the soul acts upon the body, but inferred that it must do so through the nerves which, he said, are "composed of a certain medullary substance full of juice, with a double membrane which surrounds that substance; and also an infinite number of little cords within these membranes and medullary substance, extended from their beginning to the very extreme capillaments, which are dispersed and inserted into various parts of the muscles." Croone's beliefs concerning muscular contraction changed somewhat in the course of his life, and it seems best to give his theory in its final form, as briefly described in his lecture read at the Surgeons Theatre in 1674-75. He published the following summary of this lecture in Hooke's *Philosophical collections.*[4]

---

[2] Birch, T. *History of the Royal Society,* vol. 1, p. 422, 1756.

[3] Croone, W. *De ratione motus musculorum.* London: J. Hayes, i+34 pp., 1 pl. (anon). In the same year and again in 1666 the work was appended to an 8° edition of Willis's *Cerebri Anatome,* published in Holland and erroneously attributed to this author. A

An Hypothesis of the Structure of a Muscle, and the Reason of its Contraction; read in the Surgeons Theatre Anno 1674, 1675. by Dr. C.

Having shewn and proved at large, That the motion of a *Muscle,* is performed only by the Carnous *Fibres,* and that each distinct Carnous *Fibre* had a power of Contracting it self; I offered an *Hypothesis* of the Structure of one Carnous *Fibre,* since the force of the whole *Muscle* is but an Aggregate of the Contractions of each particular *Fibre*: And this I did in farther Explication of an Hypothesis, printed in the year 1664, grounded on an Experiment made for that purpose before the *R.S.* a little before that time. In that printed Paper 'twas said, a *Muscle* in Contraction swell'd like a Bladder blown up, which would raise a great weight according to the Experiment shown to the Society: An Objection rose, That we did not see any such conspicuous swelling in the Belly of a *Muscle;* to answer which, and explicate the *Hypothesis* more clearly, I made this farther addition.

1. I supposed each distinct Carnous *Fibre* as A E F to consist of an infinite number of very small *Globules,* or little Bladders, which for explication sake I here express as so many little Triangles, *e.g.* four in this *Fibre,* A L B, B M C, C L D, D O E, all opening into one another at the Points A, B, C, D, E.

---

fourth edition signed, also in Latin, appeared in Amsterdam in 1667 from the press of Caspar Commelinus.

[4] Hooke's *Philosophical Collections,* no. 11, sec. 8, pp. 22-25, 1675. Hooke's "Collections" was a private publication which filled the gap during the years that the *Philosophical Transactions* of the Royal Society had been abandoned owing to lack of funds. Croone's lecture was also published (in Latin) in the *Acta Eruditorum* (1682, pp. 194-197.)

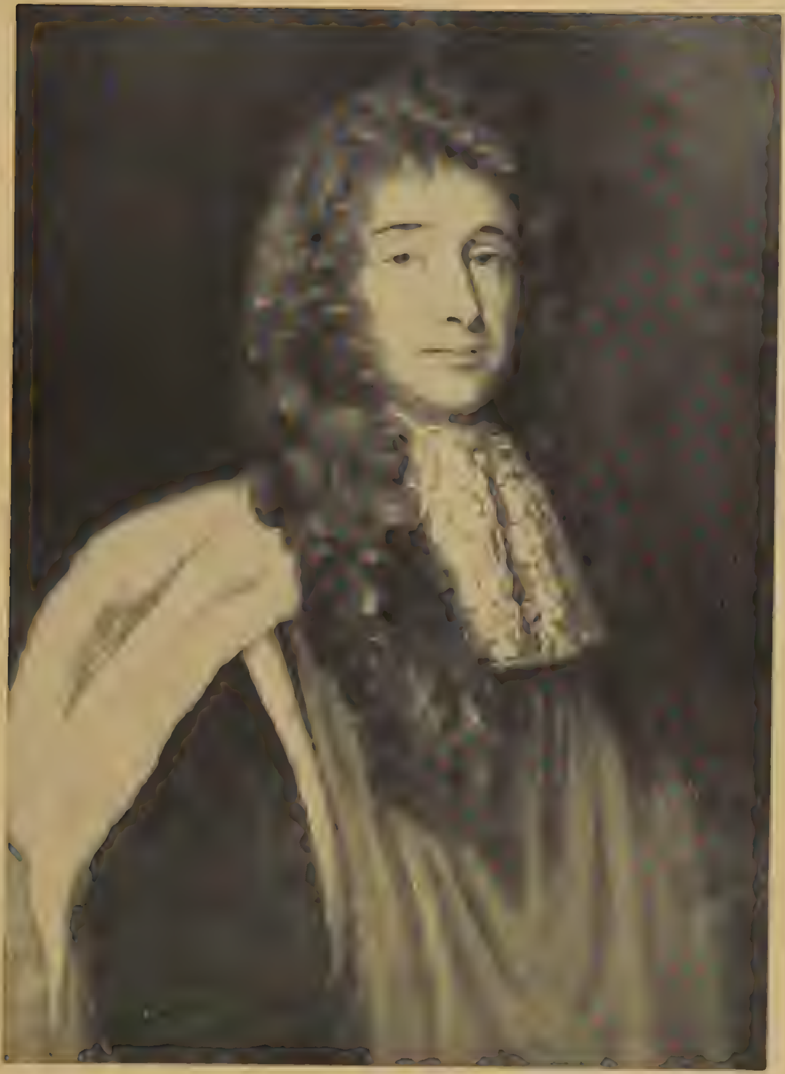
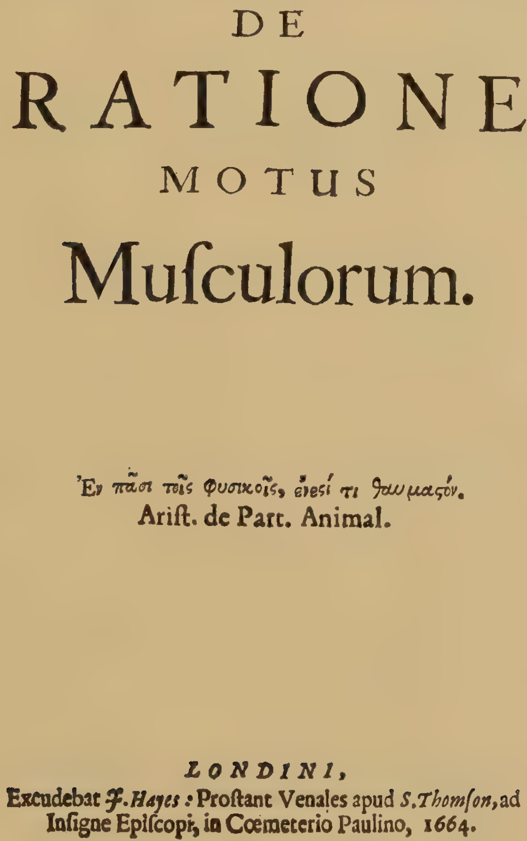


FIGURE 39. William Croone (1633-1684). The portrait which hangs in the Censor's room at the Royal College of Physicians, London (obtained through the courtesy of the College).

2. I did not only suppose, but endeavoured to prove, That from the *Artery* of each particular *Muscle,* the nourishing Juice of the *Muscle* was thrown out and extravasated to run at large among the Carnous *Fibres,* and insinuating it self by the constant Pulse of the Heart was driven on, and after mixing with another Liquor it meets with between the *Fibres* in the *Muscles,* came to be strain'd through the Coat of each Globule or little Bladder into the Cavity of it: And likewise, that from each ramification of the *Nerve* within the *Muscle,* that second sort of Matter much more fluid and active than the former is extravasated, and these mixt together as I said, enter into each little Bladder, and by these constant agitations, ebullition, or effervescence, which with the natural heat that is partly the cause, and partly the constant assister of



DE

RATIONE

MOTUS

Muſculorum.

Ἐν πᾶσι τοῖς φυσικοῖς, ἐνεςί τι θαυμαςόν.
Ariſt. de Part. Animal.

LONDINI,
Excudebat *J. Hayes* : Proſtant Venales apud *S. Thomſon,* ad
Inſigne Epiſcopi, in Cœmeterio Paulino, *1664.*

FIGURE 40. The title-page of the first edition of Croone's anonymous tract on muscular motion.

this motion, and makes that which we call the very life of every part, as long as the Animal lives, keeps these Globules or small Vesicles always distended. How it enters in, and sends out its effete Particles again into the mass of Blood to be discharged by Transpiration, and every moment takes in fresh, I endeavoured in those Lectures to shew at large.

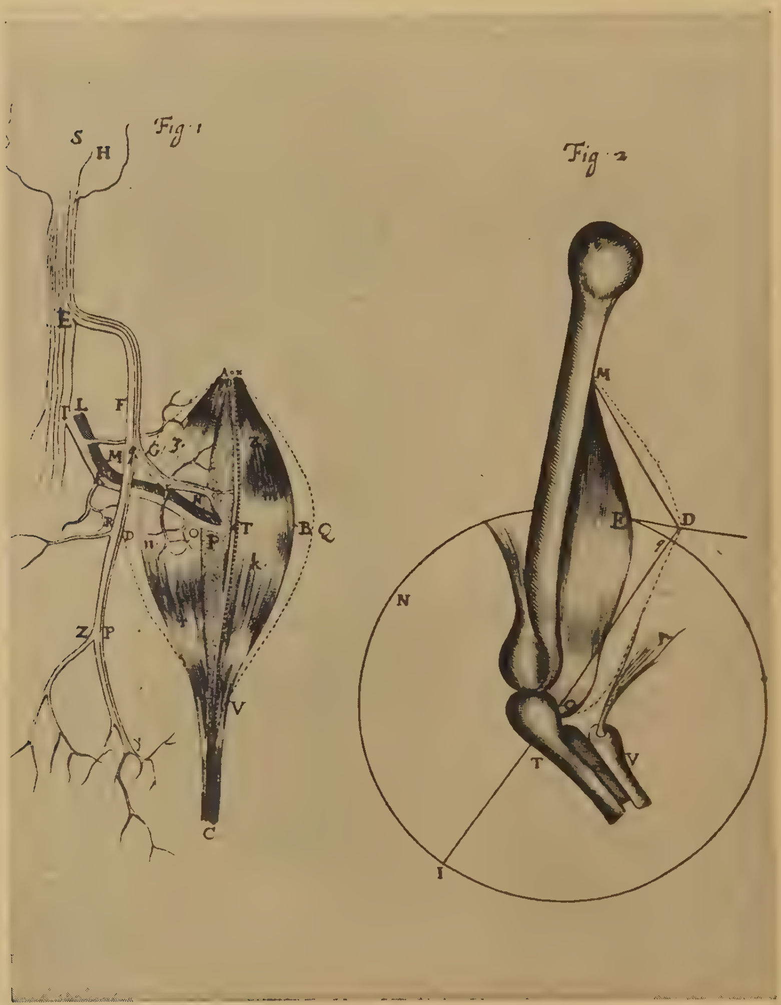


Figure 41. Croone's diagram illustrating his beliefs concerning the relation of the circulation and nerve supply of muscle to contraction and the direction of forces exerted by certain muscles at the elbow (from the *De ratione motus musculorum,* 1664).

3. By the aforesaid agitation each little Bladder A L B, B N C, *&c.*

is always as I said distended more or less, as long as the Animal has life or warmth.

4. The Force or Energy of which distention to contract the *Fibre* A F, either into it self from both extremes A and F, or if A be fixt from F, and so to raise with it any weight, as that at F to E, or any Limb as Fig. Bicep. the Arm and Hand C, was before demonstrated in the printed Paper, and in an Experiment entered in the Journal of the Society.

5. By these four small Bladders, I answer the fore-mentioned Objection, which was made against the Principle laid down in the printed Paper, and show that the *Fibre* A F (and so of the whole *Muscle*) does not distend it self as one single great Bladder A K E from *C* to K in raising the weight from F to E, but those innumerable small Bladders are each distended but a very little imperceptible space, and yet produce the same effect to raise a weight from F to E. As if we suppose four little Bladders only for Example sake, each of them being distended from Q to L, shall all together raise the weight F to E, as well as one great one swelling from C to K: The Demonstration is easie; for since both the four little Bladders A L B, *&c.* and the great one A K E before distention, made the whole *Fibre* A F, supposing a like distention both in the little ones and great one, the Angle B A L will be equal to E A K, and A L B to A K E will be alike, and have their sides proportional; and the same may be said of A L Q and A K C. Then because while A K E was undistended, the Point E was lower in F; likewise A L B undistended must have the Point B lower, as suppose in P, and also because A P is equal to A K E *ex Hyp.* therefore *as* A L B. A K E : : A P. A F, but A L B. A K E : : A B. A E: If therefore from the Proportionals A P, A F, you take like Proportionals A B, A E; the Remainder B P, E F, shall be like Proportionals, but A L B is ¼ of A K E *ex Hpy.* Therefore P B is ¼ E F; then likewise each of the other three little Bladders will raise the Weight one Fourth, and so the four Fourths being equal to E F altogether will raise the weight the same height with the great one A K E single; and that with one Fourth of the distention or swelling, for 'twas prov'd Q L was ¼ of C K. Now if instead of four little Bladders in a *Fibre,* we substitute 4000 that *Fibre* shall raise the Weight in the space E F with $^1/_{4000}$ part of the swelling; and so of $^1/_{400000}$, *&c.*

6. Hence was at large shown: 1. The manner of the Blood's Circulation in each particular *Muscle,* what it contributed to this Motion. 2. What the Perspiration out of each *Muscle* did towards it. 3. That

there was some swelling in the Contraction of each *Muscle.* 4. How every *Muscle* in contraction grows more hard, dense, and compact. 5. The necessary cause of every *Muscle* having its Antagonist. 6. Why on a Paralysis or wound of one side, the Antagonist presently contracts. 7. Why upon Fractures it runs up. 8. Why in Animals kill'd, while the Flesh is warm there appear so many jerks and contractions of Muscles. 9. Why a Muscle cut in the middle runs up to each end, *&c.* These and several other Particulars I did endeavour to make out at large in those Lectures; yet only in the way of an Hypothesis, not as if I did presume to believe I had found out the true secret of *Animal Motion,* when I am almost persuaded, no Man ever did or will be able to explicate either this or any other *Phenomenon* in Nature's true way and method: But because I reckon such Speculations among the best Entertainments of our Mind, I may chance to collect and publish sometime or other what I then said, and have lately try'd about it. And I am the more willing, First, because Mr. *Lewenhook* has since told us, That he finds by his Microscope the Texture of a carnous Fibre to be of innumerable small Vesicles or Globules, which gives an appearance of reality to the said Hypothesis, and them, [sic] because a sheet or two, and two or three schemes, of that long expected Work of *Borelli, de Motu Animalium,* having been sent to the *Royal Society,* I find there some Schemes for explicating Muscular Motion, the very same with those I make use of; and the same Experiment of the Bladder applied in another Scheme to this occasion likewise: How he has explain'd or manag'd them, as yet I know not, but his using them, has made me have a better opinion of this Thought than else I should ever have had; and if ever I reprint and enlarge that Pamphlet, *de Ratione Motus Musculorum,* I would not be thought to have made use of what was another's for my own. Lastly, when the Publisher told me, he intended in his next *Philosophical Collections* to give an account of *Borelli's* Book, and also if I would to insert this Paper, I was for the same reason the more willing to accept of that favour from him.

THOMAS WILLIS

THOMAS WILLIS (1621-1675) is a much underrated contributor to physiological literature. His methods of experiment and his process of reasoning were sometimes erratic, and did not conform with the standards set by some of his contemporaries such as Boyle and Lower. Yet Willis had wide clinical experience, he recorded what he saw and he frequently gave evidence of penetrating vision. His description of the anatomy of the brain, though inaccurate in places, is at times masterly, and those who now read his tracts on scurvy and on

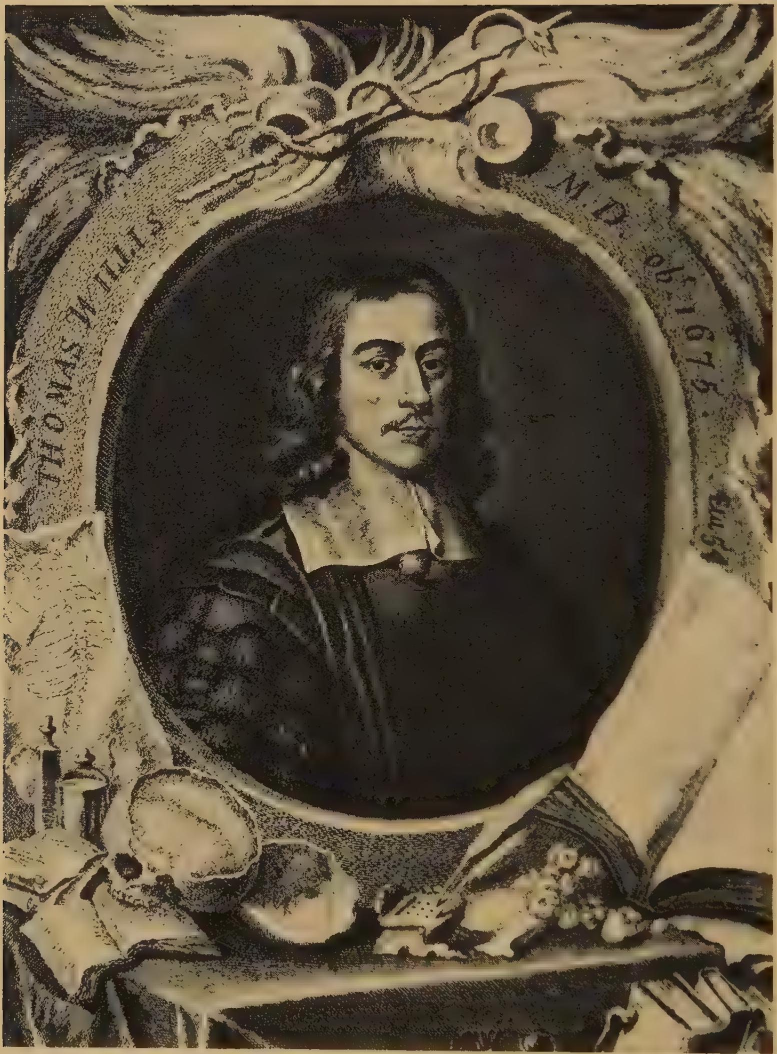

THOMAS WILLIS M.D. ob. 1675. Æt. 54

FIGURE 42. Thomas Willis (1621-1675), the discoverer of the circle of Willis.

nervous diseases will detect his shrewd powers of observation. Much given to speculation he often weakened the value of his arguments, but this should not prevent us from recognizing the nature of his achievement. His tract on muscular motion which first appeared in 1670 in Latin as an appendix to his treatise on melancholia was translated into English and appeared in London in 1684 in *Dr. Willis's practice of physick, being the whole works of that renowned and famous physician: .... fitted to the meanest capacity by an index.* We have found this translation particularly useful. The following passage[5] indicates that Willis made experiments for himself, but it also illustrates his tendency to speculation.

As often as the motion of a living Muscle was beheld by me, I considered and weighed in my mind by what means all the fleshy fibres were contracted and released by turns, I could conceive or collect no other thing than that in every contraction, the Spirits or certain elastick Particles did rush into the fleshy fibres from either Tendon, and did intumifie and force them nearer towards themselves or together; then the same Particles presently coming back from the flesh into the Tendons, the relaxation of the Muscles happened. In a bare or naked Muscle, when I had separated every fleshy fibre or a company of them apart from the rest in the whole passage by help of a Microscope, I most plainly perceive the Tumor, begun at either end of the flesh, to be carried towards the middle, as it were by the Spirits, entred here and there at once. Further (which I mentioned before) each fibre being tyed about the middle, being as it were as yet free and compacted with the others, was contracted or drawn together; but a Ligature being put to both ends, is remained flaggy constantly above or beyond the bound place. But that I might no longer doubt concerning this, I applied two Ligatures, at equal distances from the middle and the ends, about the same bundle of fleshy fibres, which being done, a contraction and swelling up arising presently from either fleshy extreme to the places bound, went no farther; the middle part between in the mean time being unmoved, remained flaccid; whence it may be well concluded, that in every musculary contraction the animal Spirits or elastick Particles do leap out from the tendinous fibres into the fleshy, and vicissively in the relaxation, recede or run back from these into those.

However this being proved and granted, there yet remain very many difficulties concerning Musculary Motion; for first, it may be asked how the animal Spirits, which enter silently, or without any incitation, or Tumor, the tendinous fibres do so blow up the fleshy fibres, that they are able to force them altogether into shorter spaces.

---

[5] Willis, T. *Affectionum quæ dicuntur et hypochondriacæ pathologia spasmodica vindicata contra. . . . . N. Highmorum. Cui acceserunt exercitationes medico-physicæ duæ: 1. De sanguinis accuncione. 2. De motu animalium.* London: 8°; 2nd ed., 1670; *Leiden.* 12°. 1671.

But that the fleshy belly of the Muscle, whilst it is contracted, doth swell up, is not at all to be doubted, because this is evidently beheld by the sight and touch in the dissection of living Creatures: to wit, all the fleshy fibres being wrinkled together, are made more tumid and sharper, and so shorten the Muscle, and make it also thicker and broader: For the more certain belief of this, when I had bound some of the fleshy fibres, separated from the knitting of the rest, and had left others near them loose, there appeared a notable difference between those flaccid or not swelled, and these intumified or swelled up in every contraction of the Muscle.

But if it be demanded, of what nature, to wit, whether spirituous saline, as may be believed, or of any other disposition, the animal Spirits, derived from the Brain into the Muscles, may be; and then whether the other Latex, immediately carried to them from the blood, is sulphureous or nitrous. Concerning these, because it appears not to the sense, we shall pronounce nothing rashly or positively. But even as in other natural things, the active Particles of a various kind, which being unlike among themselves, are found apt mutually to grow hot, or to be struck off from one another, otherwise to be rarified or expanded; and as the intestine motions of Bodies, and especially the elastick, such as are the contractions of the Muscles, can only proceed from the congressions of such like, certainly it may be lawful to presume, that these do wholly depend upon such a cause.

Therefore as to the Musculary Motion in general, we shall conclude after this manner, with a sufficiently probable conjecture, *viz.* that the animal Spirits being brought from the Head by the passage of the Nerves to every Muscle (and as it is very likely), received from the membranaceous fibrils, are carried by their passage into the tendinous fibres, and there they are plentifully laid up as in fit Store-houses; which Spirits, as they are naturally nimble and elastick, where ever they may, and are permitted, expanding themselves, leap into the fleshy fibres; then the force being finished, presently sinking down, they slide back into the Tendons, and so vicissively.

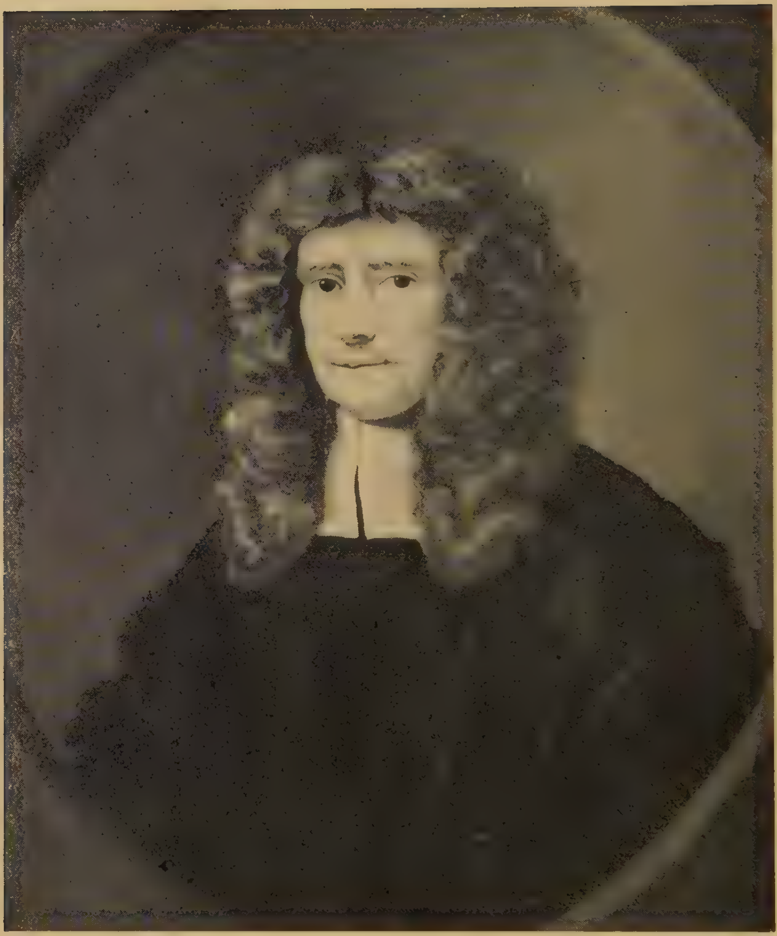


FIGURE 43. Francis Glisson (1597-1677). The Bodleian portrait which now hangs in the Radcliffe Scientific Library, Oxford (obtained through the courtesy of Bodley's Librarian).

FRANCIS GLISSON

Francis Glisson (1597-1677), Regius Professor of Physic at Cambridge from 1636 until his death, is remembered for his description of the fibrous sheath of the liver, still known as Glisson's capsule, and for having written the first authoritative monograph to be published in England on a single disease (Rickets, 1651). In physiology Glisson is remembered more especially for the theory of irritability and for being the first to oppose the then prevalent theory of animal spirits as a cause of muscular contraction. The following passage is his description of an experiment indicating that the volume occupied by muscle during contraction did not increase, but in point of fact, seemed actually to diminish.[6]

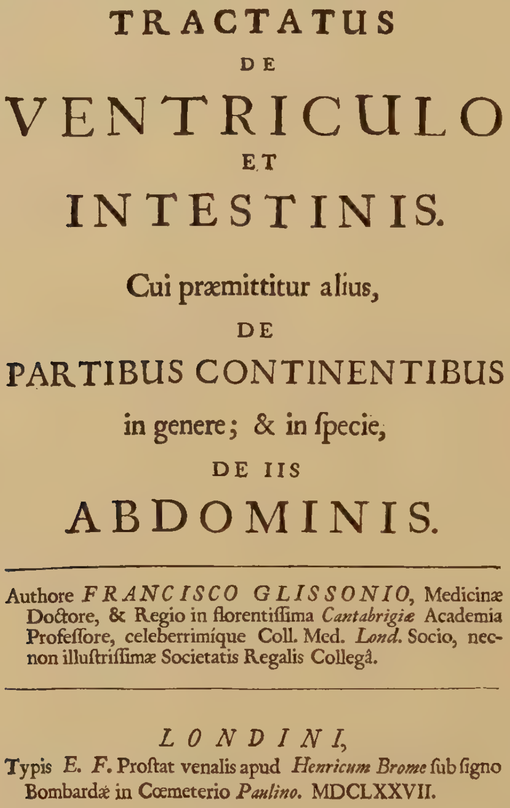
MUSCLE VOLUME CONSTANT DURING CONTRACTION

I come to the second important reason proving animal spirits not to be the immediate cause of sense and movement. The flux and reflux of matter in the same channels is rarely to be met with in nature's arrangements. In breathing, expiration and inspiration go on in the same organs, but the cartilaginous windpipe was made for that purpose, and the thorax is in turn both contracted and dilated. The fact of the flux and reflux of the intestinal juices is admitted but the peristaltic movement is provided for the same purpose, *i.e.* for repeatedly shifting the chyle. But in the nerves there is hardly sufficient cause to show why the spirits should sometimes be carried inwards and sometimes outwards, unless in the nerves too we assume a peristaltic movement or think that the animal spirits, just as if they were small tubes, run both up and down, and, according as they have the mastery, now flow out and now back. But they go forth to nourish the parts and determine the organs of sense according to their suitable functions. The sensation of the same objects sometimes lasts several hours. Do the animal spirits in the nerves both go forth and return during the whole of that time so that the object of sensation continues a long time in both the outer and inner organs? I cannot solve these riddles. Moreover the object of these spirits is to inflate the fibres into movement; indeed, the muscles contract in length as they swell in breadth and move the bones joined to the tendons. However, as a result of the following experiment, the idea of the explosion of spirits and of the inflation of muscles has for some time now been silenced.

Take an oblong glass tube of suitable size and shape, and in its side at the top near its mouth, fix another upright tube shaped like a funnel. Get a strong brawny man to thrust the whole of his bared arm into the opening of the larger tube, and then let the opening of the tube be luted up all round the man's shoulder so that no water can escape: then pour through the funnel as much water as the glass can hold and in the water in the tube, so far from sinking, would rise. Therefore one addition allow some water to overflow into the funnel. When this has been done, order the man now in turn to contract strongly, and now to relax, all his arm muscles. During contraction the water in the tube sinks, but during relaxation rises. Hence it is clear that the muscles when taut and contracted, are not inflated or swollen, but are on the contrary unswollen and actually diminished. For if they were swollen,

---

[6] Glisson, F. *De ventriculo et intestinis. Cui præmittitur alius, de partibus continentibus in genere; & in specie, de iis abdominis.* London: Henry Brome, 15 leaves, 509 pp., 1 leaf, 1677 (Chap. 8, para. 9-10, pp. 166-168).



TRACTATUS
DE
VENTRICULO
ET
INTESTINIS.

Cui præmittitur alius,
DE
PARTIBUS CONTINENTIBUS
in genere; & in ſpecie,
DE IIS
ABDOMINIS.

Authore *FRANCISCO GLISSONIO*, Medicinæ Doctore, & Regio in florentiſſima *Cantabrigiæ* Academia Profeſſore, celeberrimíque Coll. Med. *Lond.* Socio, necnon illuſtriſſimæ Societatis Regalis Collegâ.

LONDINI,
Typis *E. F.* Proſtat venalis apud *Henricum Brome* ſub ſigno Bombardæ in Cœmeterio *Paulino*. MDCLXXVII.

FIGURE 44. The title-page of Glisson's book on the stomach and guts, in which is recorded his memorable experiment on the constancy of muscle volume during activity. In this work also Glisson sets forth at length his theory of irritability.

must conclude that the fibres are shortened by their own activity, and have no need of a plentiful afflux of animal or vital spirits by which they are inflated, for this process of shortening, and for obedience to the movements ordered by the brain.

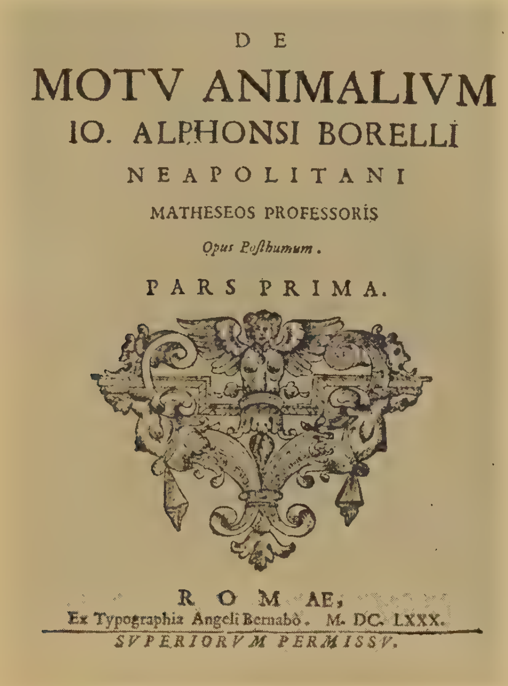
I fear lest, in this digression concerning animal spirits, I have been rather irksome to my readers, but obviously I could not avoid it nor put more succinctly what had to be said. Although I have touched lightly on the heads of the discussion only, yet the work has grown in size beyond my expectations. Now I return to the main theme and I shall try to elucidate another doubt previously mentioned, namely how the wishes of the brain communicate themselves to the nerves whose function it is to execute them.

Para. 10. The second uncertainty is whether the nerves recognise, by natural perception or sense, the particular movement of the brain above described by which they are excited, or the fibres the movement of the nerves. That I may lead no other mind but my own into error, I warn readers that every complete action that has its origin in sense and sensory desire is animal in its particular feeling, and similarly what proceeds immediately from the understanding and will is free. I have said in my book "De vita naturae," Chapter 15, n. 3, that there are three successions of vital faculties, and that the perceptive faculty among them is the leader of the others. Here I must say again that the natural faculties are frequently confused with the sense faculties, and these again with the intellectual in the same complex operations. But in this occurrence the whole action is generally named from the higher faculties. But if the same process originates with a higher faculty, however much the lower faculties also are subject to its sway, it is still named from the former only. However, we must not overlook in the evolution of the whole action the contribution made by the lower faculties in fulfilling that same action. The present investigation can be taken as an example in which, although we have agreed that the whole action is animal because it has its origin in sense and sensory desire, yet we are not thereby prevented from asking whether in its production, some natural actions are connected with it. Indeed, we are not examining the whole matter sufficiently thoroughly unless we accurately investigate what kind these actions are. Therefore, granted these premises, I say that the brain notices its own movements, the nerves the brain's movements and the fibres the nerves' movements, not by sense but by natural perception alone. I think that the truth of all this can be shown by one argument. We judge that whatever we recognise by sense, we feel because the sense has drawn our attention to it. Indeed whatever we seek by sensual desire we obviously apprehend with our inner senses also, so that no animal operation is altogether concealed from our senses; but the brain, when stimulated by its own desire and when moving outwards to accomplish that desire, is not aware by sense that it moves thus, nor does it distinguish by sense in what way it communicates its movements to the nerves to which it goes. Similarly the nerves are not aware of the movement which they communicate to the fibres they stimulate. Finally the fibres do not distinguish by sense their excitability at the movement stimulated by the nerves. They are aware of all this by natural perception alone and by its medium are the respective parts stimulated to the performance of their various functions. For the muscle, with regard to the stimulus it feels, is obviously unaware by what means or by what agents it is set in motion by the brain.

Let there be provided a Glass Tube, in Length and Bore capacious enough to hold a Man's Arm, and to the upper Orifice of it on the Outside affix another Tube of Glass about an Inch Diameter in Bore, shaped like a common Weather-glass, only with a wide Mouth like a Funnel; so as the Lower-end may open into the greater Tube whose Bottom is firmly stopt: Then having erected both Tubes, let a Man of strong and brawny Muscles thrust his whole naked Arm into the greater Tube up to the very Shoulder, about which the Orifice of the Glass must be closely luted, that no Water may flow out that way. This done, let as much Water be poured in by the Tunnel as both Glasses will receive, leaving only a little Space at the Top of the lesser, empty. In fine, let the Man strongly contract all the Muscles of his Arm by clinching his Fist, and relax them again by Turns; and you shall abserve, that when he contracts his Muscles, the Water in the less Tube will sink somewhat lower, but rise again when he relaxes them: Whence it is evident, that the Muscles do not swell up, nor are inflated at the time of their Contraction, but rather are lessened and contracted in all their three Dimensions; otherwise the Water would at that time, not descend, but ascend in the Neck of the Funnel.

GIOVANNI ALFONSO BORELLI

Giovanni Alfonso Borelli (1608-1679), the author of the "De motu animalium" is included in this series of readings not for any important discovery, but rather because of the influence which he exerted upon this field of work. His book, an enormous work in two volumes, contains an analysis of the mechanics of contraction: how muscles act at joints, what tension they must develop in order to overcome a given mechanical disadvantage, etc. It also contains interesting observations upon reciprocal innervation and tonus. His theory of contraction, though little in advance of Galen, is of some interest as showing the influence which the new chemistry of his day had already exerted. This is well illustrated in the following selection.[7]



DE

MOTV ANIMALIVM

IO. ALPHONSI BORELLI

NEAPOLITANI

MATHESEOS PROFESSORIS

Opus Poſthumum.

PARS PRIMA.

ROMAE,

Ex Typographia Angeli Bernabò. M. DC. LXXX.

SVPERIORVM PERMISSV.

FIGURE 45. The title-page of the first volume of Borelli's book on the movements of animals.

Since all muscles, with some few exceptions, do not manifest vital movement otherwise than in obedience to the will, since the commands of the will are not transmitted from the brain which is the instrument of the sensitive, and the seat of the motive soul, by any other channels than the nerves as all confess and as the most decided experiments shew, and since the action of any incorporeal agency or of spirituous gases must be rejected, it is clear that some corporeal substance must be transmitted along the nerves to the muscles or else some commotion must be communicated along some substance in the nerves, in such a way that a very powerful inflation can be brought about in the twinkling of an eye. And since the inflation, hardening, and contraction do not take place in the channels which serve for bringing them about and in which the motor influence resides, namely, in the nerves themselves, but takes place outside the nerves, namely, in the muscles, it is evident that the substance or the influence which the nerves transmit is not taken by itself alone sufficient to bring about that inflation. It is necessary, therefore, that something else must be added, something which is to be found in the muscles themselves; or that in the muscles there is some adequate disposition of material so that on the arrival of the influence transmitted by the nerves there takes place something like a fermentation or ebullition, by which the sudden inflation of the muscle is brought about. That such an action is possible is rendered clear by innumerable experiments which are continually being made in chemical elaborations as when spirits of vitriol are poured on oil of tartar; indeed all acid spirits when mixed with fixed salts at once boil up with a sudden fermentation. In like manner, therefore, we may suppose that there takes place in a muscle a somewhat similar mixing from which a sudden fermentation and ebullition results, with the mass of which the porosities of the muscle are filled up and enlarged, thus bringing about the turgescence and the inflation.

---

[7] Borelli, G. A. *De motu animalium.* Rome: Angelo Bernabo, 2 vols., 3 leaves, 376 pp., 6 leaves; 1 leaf, 520 pp., 1681 (prop. 14-18, selections translated by Foster).

In the same way, if one of the extremities of the nerve fibre be compressed or pushed, or struck or pinched, forthwith the commotion and concussion or undulation ought to be communicated right to the other end, because by reason of their contiguity, the parts lying first in an ordered series by pressing on those following, communicate the blow and the impulse right to the end. Hence it follows that the fibres or spongy ducts of certain nerves turgid with the spirituous juice can be shaken or pinched by that gentle motion of the spirits by which the acts of the command of the will are in the brain carried out, and then, by concussing the whole length of the nerve through the convulsive irritation, can squeeze out and discharge from their extreme orifices some spirituous droplets into the appropriate muscle, whence the ebullition and explosion follow by which the muscle is contracted and rendered tense.

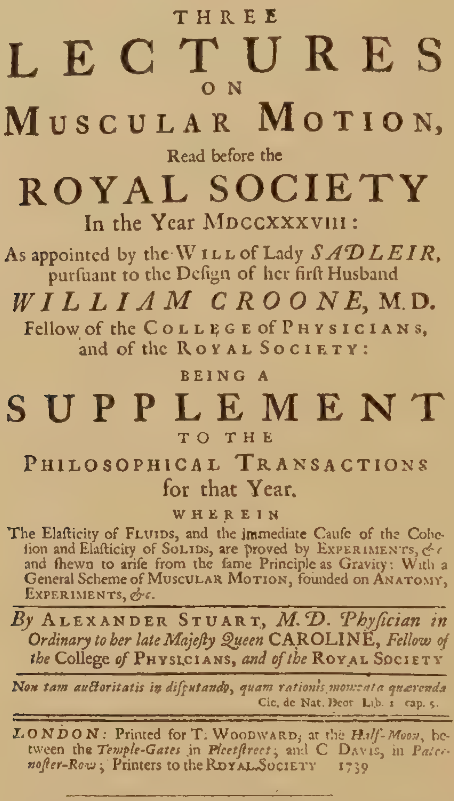
And on the other hand when the extremities of the sensory nerves which end in the skin, nose, ears or eyes, are compressed or struck or titillated, it necessarily follows that forthwith the concussion, undulation, or titillation of the spirituous juice contained within the tubules is conveyed along the whole length of the nerve and reaches the particular part of the brain to which the nerve fibres are joined. And here the faculty of the sensitive soul according to the region of the brain thus percussed, according to the vehemence of the blow and the fashion and mode of the motion, is able to form a judgment concerning the object causing the movement. [He insists that the] juices, however spirituous and active, are always corporeal and cannot act at a distance, and cannot, without physical contact, increase, intensify, or depress the animal spirits; it is by means of their corporeal presence that they either increase the animal spirits which are also corporeal, mixing themselves with them, or expel them, or transform them. Wherefore it cannot be conceived that nervous action can take place without some local movement of the nervous juice passing along the whole length of the nerve right to the brain.

Concerning the fluid of muscles how uncertain, or rather how wholly wanting, is our knowledge. Fluid certainly exists in the fibrillae of which the motor fibres are composed and between the fibrillae, also between the motor fibres themselves, in the membraneous fibrillae [that is the connective tissue], and between the membraneous fibrillae; but in truth it is by no means clear whether these fluids are all of one kind or whether just as they are distinct in the seats which they occupy so they differ in material properties.

Nor is it known whether any of these fluids are really like any one of the fluids so far known to us. Animal spirits, the more subtle part of the blood, the vapour of blood, and the juice of the nerves, these are names used by many, but they are mere words, meaning nothing. Some going further bring forward saline and sulphureous particles or something analogous to spirits of wine. Such things may perhaps be true, but are neither certain nor adequately distinct. Experience teaches us that a dose of spirits of wine restores exhausted powers, but who shall have determined whether that which restores the fluid spirit is to be ascribed to this said humour which we call spirit or to some other material or is joined to it through some other cause?

As the substance of this fluid is unknown to us, so is its movement undetermined, since neither by sure reasoning nor by experiment has it been ascertained whence it comes whither it tends, where on its departure it betakes itself. . . . .

There remains another difficulty of no less moment not yet cleared up, namely in what respect the movement of the fluid in a muscle while it is contracting differs from the movement of the fluid in the same muscle when it remains quiet, uncontracted. Is its quantity changed? or does it remain the same? Is the fluid after the event, supposing it remains, the same as before the event? Does the fluid move because the muscle contracts, or does the contraction of the solid proceed from the movement of the fluid? (Foster's translation)



THREE
LECTURES
ON
MUSCULAR MOTION,
Read before the
ROYAL SOCIETY
In the Year MDCCXXXVIII:
As appointed by the WILL of Lady *SADLEIR*,
purſuant to the Deſign of her firſt Husband
WILLIAM CROONE, M.D.
Fellow of the COLLEGE of PHYSICIANS,
and of the ROYAL SOCIETY:
BEING A
SUPPLEMENT
TO THE
PHILOSOPHICAL TRANSACTIONS
for that Year.
WHEREIN
The Elaſticity of FLUIDS, and the immediate Cauſe of the Cohe-
ſion and Elaſticity of SOLIDS, are proved by EXPERIMENTS, *&c*
and ſhewn to ariſe from the ſame Principle as Gravity: With a
General Scheme of MUSCULAR MOTION, founded on ANATOMY,
EXPERIMENTS, *&c.*

By ALEXANDER STUART, *M.D. Phyſician in*
Ordinary to her late Majeſty Queen CAROLINE, *Fellow of*
the College *of* PHYSICIANS, *and of the* ROYAL SOCIETY

Non tam auctoritatis in diſputando, quam rationis momenta quærenda
Cic. de Nat. Deor Lib. 1 cap. 5.

LONDON: Printed for T. WOODWARD, at the *Half-Moon*, be-
tween the *Temple-Gates* in *Fleetſtreet*; and C DAVIS, in *Pater-*
noſter-Row; Printers to the ROYAL SOCIETY 1739

FIGURE 46. The title-page of the first Croonian Lecture on muscular motion, 1739.

ALEXANDER STUART

ALEXANDER STUART (1673-1742), the first Croonian Lecturer, was born in Scotland and received his M.D. from Leiden in 1711, presenting for the degree a dissertation bearing the title *De structura et motu musculare.* Stuart was Physician-in-Ordinary to the Queen and was attached to Westminster and St. George's Hospitals. The following passage[8] has been included in this volume of selected readings to show that the theory of reflex action had not at this time found its way into physiological thought, even though Descartes had already referred to it in vague and halting terms. This passage serves also to illustrate that Galenical doctrine still held sway in the field of the nervous system. The figure reproduced from Stuart's *Lectures on muscular motion* is the first to depict the familiar manœuvre of pithing a frog.

---

[8] Stuart, A. *Three lectures on muscular motion, read before the Royal Society in the year MDCCXXXVIII.* London: T. Woodward, x+54 pp., 1739 (pp. 37-39). A Latin edition of the same lecture under the title *Dissertatio de structurâ et motu musculari* was published the year before.

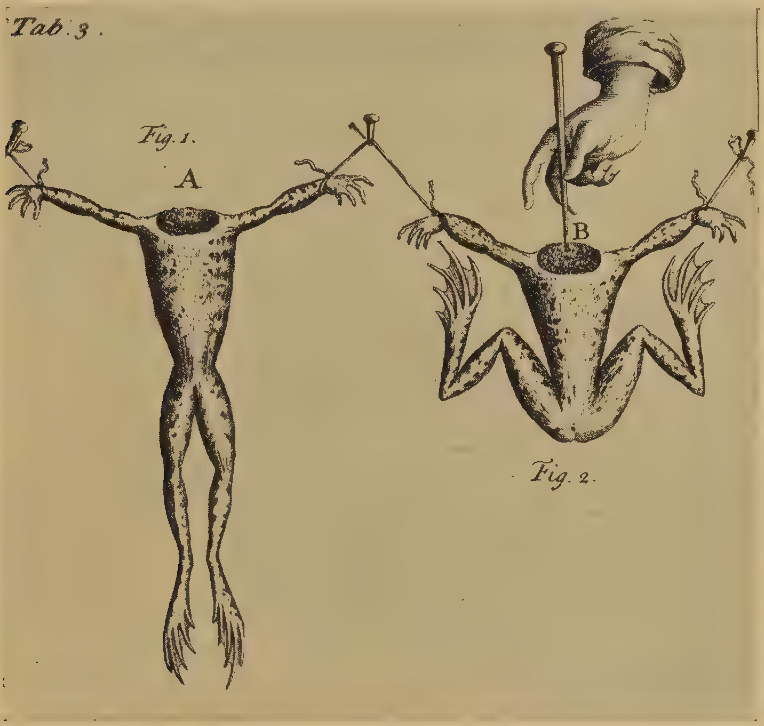

Tab. 3.
Fig. 1.
A
B
Fig. 2.

FIGURE 47. Stuart's diagram illustrating the motions induced in a decapitated frog on compression of the spinal medulla. He fancied that the movements were due to pressing fluid into the nerves (from the first Croonian Lecture, 1739).

THE MANNER, EXPLANATION AND USE OF THE Vth EXPERIMENT

1st, This Experiment is performed by suspending a live Frog by the fore legs in a frame, or in any other commodious manner, as in Tab. 3. fig. 1. when having cut off the head from the first vertebre of the neck with a pair of scissars, a small probe, the button at its extremity being first filed flat, is to be pushed very gently down upon the upper extremity of the *medulla spinalis,* in the first vertebre of the neck; upon which the inferior limbs, which hung down loose, will be immediately contracted, as they appear in Fig. 47. tab. 3. The same probe pushed gently through the hole of the occiput of the scull on the *medulla oblongata,* will make the eyes move, and sometimes the mouth to open.

2dly, The same being repeated at some small interval of a few seconds, succeeds for several times in the same manner; until the extremity of the spinal marrow be either pushed down too far out of the reach of the probe, or contused by it, which last effect appears soonest on the *medulla oblongata*: but after this the Experiment will not farther succeed, the compression then ceasing to be equal or uniform.

OBSERVATIONS ON THIS EXPERIMENT

Obs. I. It must be observed, that this Experiment succeeds better in the summer months some time after the Frogs have spawned, than it does early in the spring, or in winter when those creatures are almost dead by cold, and want of food.

Obs. 2. The interval of a few seconds in repeating this Experiment on the same Frog, seems to be necessary for recovering the equality of the circulation, which was disturbed by the immediate preceding convulsion, as it throws the blood violently out of the muscles in the time of their contraction or systole, which cannot be restored immediately in such a languid state of circulation, as this Experiment must bring on; and as the assistance of the blood will appear by the following scheme to be necessary to muscular motion, where it is deficient, the motion must also be defective or imperfect, as it appears in repeating the pushes too quick.

Obs. 3. As the inferior process of the brain called the *medulla oblongata,* and its continuation called the spinal marrow, are only a continued or prolonged collection of the nerves arising from the brain and cerebellum; by this Experiment it appears, that the nerves contribute remarkably to muscular motion; and their assistance in it is owing to the fluid they contain, I have endeavoured to prove, by shewing the non-elasticity of the nerves in the first Experiment.

Obs. 4. The motion here excited is in the muscles of voluntary or spontaneous motion, which are under the command of the will.

Obs. 5. The effect of the impulse by the probe is the same, which is or may be produced in these muscles by the mind or will; or is the very same in its manner as voluntary or spontaneous motion, and performed by mediation of the same instruments, to wit, the animal spirits, or fluid of the nerves, and the muscles of voluntary motion.

Obs. 6. The extremity of the probe applied in this Experiment being flat, cannot produce this effect by irritation, but by compression; and the compression of the pliable extremities of tubes full of any fluid, must depress or propel the contained fluid towards the lower or opposite extremities, with an increased degree of velocity. Therefore at least the beginning of this motion may be justly ascribed to a propulsion of a small quantity of the contained fluid, through these slender canals into the muscles, in which they terminate, with some greater degree of velocity, and in some greater quantity than usual. Whence we may conclude, that voluntary muscular motion in a living animal is begun in the same manner, by an impulse of the mind or will on the animal spirits through the nerves, into the muscles.

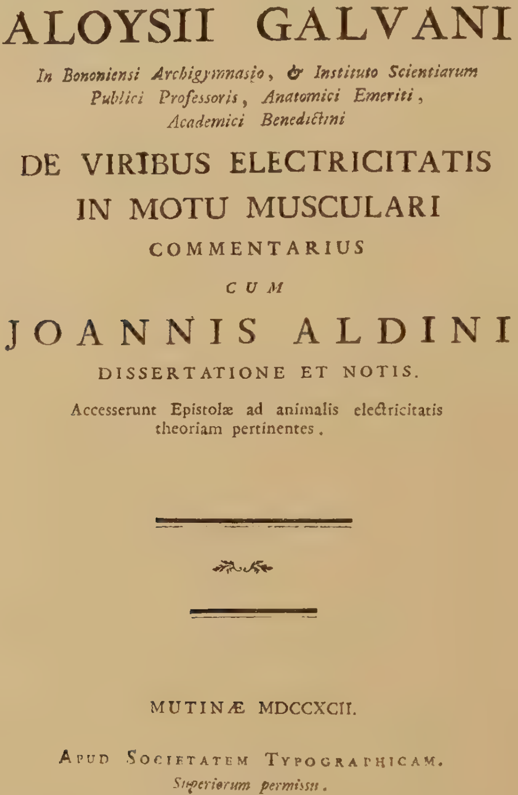
ALOYSIO L GALVANI

Aloysio L. Galvani (1737-1798), the virtual discoverer of animal electricity, was born and spent his life, as did Malpighi, in the city of Bologna. The history of his discoveries concerning "animal electricity" is confusing and difficult. Galvani's original description shows naïve enthusiasm without penetrating analysis, and it is in consequence difficult to select a passage from his own writings which gives his crucial observation. From the maze of controversy which followed the publication of the *De viribus electricitatis in motu musculari commentarius*[9] (1791), there emerged two important facts, both of which can probably be attributed with some justification to Galvani himself: (1) *The contraction with metals.*—In the passage quoted below,[10] though Galvani mentions that the blade of his scalpel was held in place by rivets of a dissimilar metal, the contraction of the frog's leg in his first experiment was clearly due to a potential conducted from the static machine. After a prolonged series of experiments it became clear that dissimilar metals when brought into contact with each other generated an electric current, and it was this in the hands of Volta that led to the great discovery of the battery and the voltaic pile. (2) *Contraction without metals.*—Galvani had maintained that contraction resulting from metallic contact was due to electricity generated within the tissue, and in his efforts to prove that electricity could in fact be generated by animal tissues he found that if a nerve were made to touch another tissue at two points, one injured and one uninjured, the muscle supplied by the nerve would be thrown into contraction. This demonstrated unequivocally the existence of animal electricity. The experiment appeared in an anonymous pamphlet in 1794 which was undoubtedly by Galvani himself, since a manuscript of it in his own handwriting is known to have existed. His nephew Aldini, however, claimed authorship after Galvani's death.

---

[9] It is strange that Galvani's original book, which is in Latin, has never been translated into English or French. A German translation by von Mayer is said to exist (du Bois Reymond) but I have never seen it. A full description of the tract, however, is given by Alexander von Humboldt *Versuche über die Gereizte Muskel und Nervenfaser,* 2 Bd., Berlin, 1797; and C. H. Wilkinson *Elements of Galvanism,* 2 vols., London, 1804; J. Cuthbertson *Practical electricity and Galvanism,* London, 1807; J. Bostock *Account of the history and present state of Galvanism,* London, 1818.

[10] Galvani, A. *De viribus electricitatis in motu musculari commentarius cum Joannis Aldini dissertatione et notis. Accesserunt epistolæ ad animalis electricitatis theoriam pertinentes.* Mutinæ: apud Societatem typographicam, 12 leaves, 80 pp., 3 plates, 1792 (pp. 2-3).



ALOYSII GALVANI

In Bononiensi Archigymnasio, & Instituto Scientiarum
Publici Professoris, Anatomici Emeriti,
Academici Benedictini

DE VIRIBUS ELECTRICITATIS
IN MOTU MUSCULARI
COMMENTARIUS
CUM
JOANNIS ALDINI
DISSERTATIONE ET NOTIS.

Accesserunt Epistolæ ad animalis electricitatis
theoriam pertinentes.

MUTINÆ MDCCXCII.

APUD SOCIETATEM TYPOGRAPHICAM.
Superiorum permissu.

FIGURE 48. The title-page of Galvani's book on animal electricity, 1792.

The details of the difficult historical controversy between Galvani, Volta and Aldini are fully set forth in the first volume of Émile du Bois Reymond's *Untersuchungen über Thierische Elektricität,* Berlin, 1848.

CONCERNING ELECTRICAL FORCES IN MUSCULAR MOVEMENT

FIRST PART

I dissected and prepared a frog as in Fig. 2, Tab. 1 [Fig. 49] and placed it with everything else at hand on a table on which was an elec-

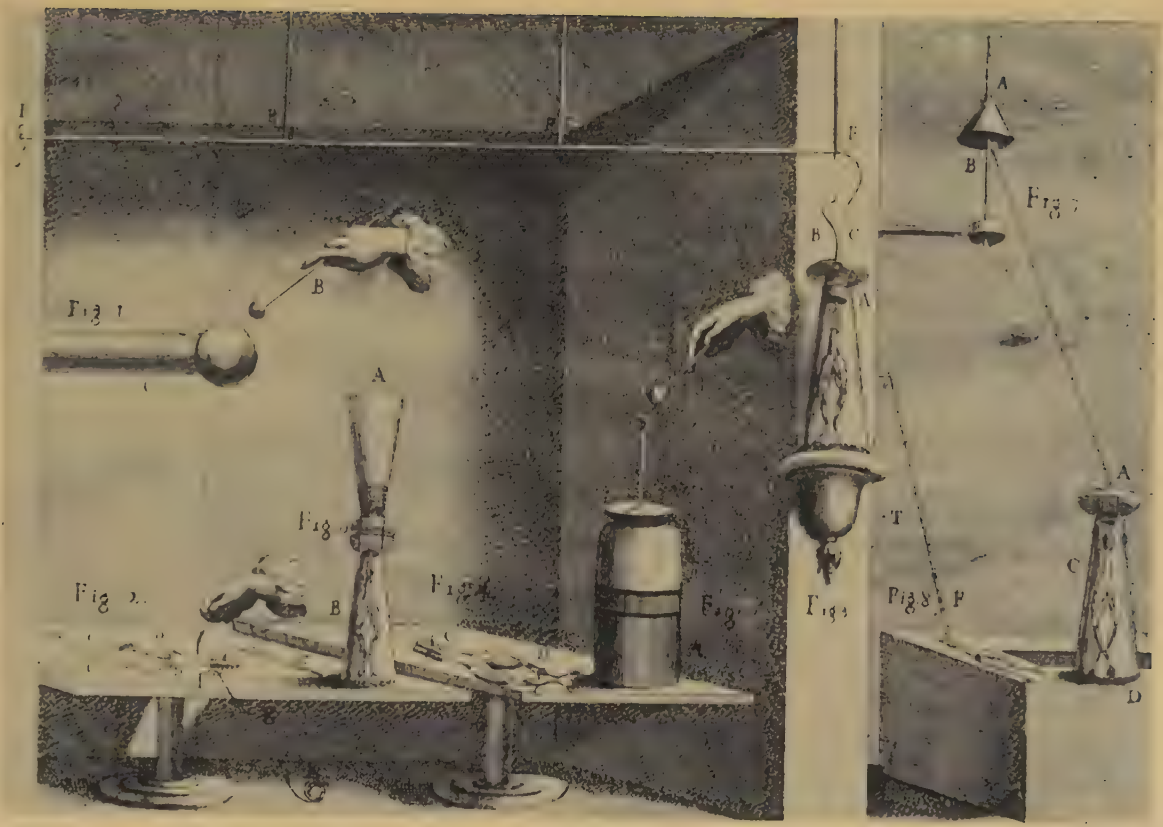


Fig 1
B
A
Fig 2
B
Fig 4
F
B
C
A
Fig 7
A
B
A
T
C
Fig 8
P
D

FIGURE 49. The figure from Galvani's book which is referred to in the passage quoted.

tric machine (see Fig. 1, Tab. 1) [Fig. 49], but the frog was completely removed from its conductor and by a considerable interval. One of those who were helping me accidently lightly touched with the point of his scalpel the inner nerve (DD) of this frog's leg, and suddenly all of the leg muscles appeared to become so contracted that they seemed to have fallen into fairly violent tonic convulsion. Another who was helping us in producing the electricity, seemed to observe that the phenomenon occurred while the spark was obtained from the conductor of the machine. He, marvelling at the novelty of the occurrence, at once drew my attention to this since I was at the time completely occupied with other things and was absorbed in my own thoughts. I was fired at once with an extraordinary eagerness and desire to perform the same experiment and to bring into the light of day the hidden secrets of the phenomenon. Therefore I myself placed the point of the scalpel on one or other of the leg nerves while one of those who were present produced a spark. The whole phenomenon was by this same means repeated, and, at the same time as the sparks were obtained, there were produced wonderfully strong contractions in each muscle of the joints just as if an animal in tetanus had been used.

But fearing that those very movements arose rather from the contact of the point which accidentally acted as a stimulus than from the spark, I tested the same nerves with the point of my scalpel by the same method in the other frogs, and indeed with greater pressure, without, however, any spark on that occasion being produced by anyone; but there seemed to be no movements at all. As a result of this I reasoned to myself that perhaps in order for the phenomenon to be established there were needed at the same time both the contact of some body and the application of a spark. Therefore I again placed the edge of the scalpel on the nerves and held it there motionless, both when a spark was produced and when the machine was absolutely still. But the phenomenon appeared only so long as the spark lasted.

We repeated the experiment always using the same scalpel, but to our amazement when the spark was produced sometimes the movements previously described took place, at other times were absent.

Stirred by the novelty of the occurrence, we began to test it by different experimental methods, always, however, using the same scalpel so that we might, if it were possible, discover the reasons for the unexpected difference. This new task was not empty of result, for we discovered that the whole matter was to be attributed to the question of which different part of the scalpel we were holding with out fingers: the scalpel had a bone handle and, if this handle were held in the hand when a spark was produced, no movements resulted, but they did result when the fingers were placed either on the metal blade or on the iron nails securing the blade of the scalpel.

Therefore since the rather dry bone produced an electric force of its own, and the metal blade and iron nails a conducting or "anelectric" force, as they say, we suspected that perhaps it happened that when we held the bone handle with our fingers all approach to the electric current, entering by some means into the frog, was stopped, but that the current was released when we took hold of the blade or the nails setting up the same current.

Therefore in order to put the matter beyond all doubt, we used instead of the scalpel first a thin glass tube (H Fig. 2) carefully polished so that all moisture and specks of dust were removed, and secondly one of iron (G). We not only touched the leg nerves with the glass but as it were rubbed them when the spark was produced, but all our efforts were in vain as no phenomenon resulted although innumerable and stronger sparks were obtained from the conductor of the machine and at a very small distance from the animal. But the phenomenon did result when the iron tube was applied to the same nerves and when quite small sparks were obtained.

[Later he found] that prepared frogs suspended by brass hooks through the spinal marrow from an iron lattice round a hanging garden of our house, exhibited convulsions not only during thunderstorms but occasionally also in fair weather. [Pursuing this experiment he later observed] when I pressed the brass hook, fixed in the spinal marrow, against the iron plate, behold! the same contractions, the same movements as before. I tried other metals with the same result, except that the amount of contraction depended on the metals used.

HENRY PICKERING BOWDITCH

Henry Pickering Bowditch (1840-1911), of Harvard, the first man in America to establish a physiological laboratory for teaching medical students, was a grandson of Nathaniel Bowditch, the distinguished mathematician and author of the "Practical navigator," and by his mother, Lucy O. Nichols, was related to Edward and William Pickering, the astronomers. After graduating from the Harvard Medical School, he studied abroad and there came under the spell of Carl Ludwig. From his laboratory at Leipzig, Bowditch published his memorable paper[11] in which the "all-or-none" principle of contraction of cardiac muscle was for the first time enunciated; in the same communication the phenomenon of the staircase ("Treppe") was described. The following passage[11] contains his description of the "all-or-none" principle.

STIMULATION OF HEART MUSCLE

The weakest induction shock which will just cause a contraction of the heart, does not evoke a minimal contraction, and the size of the contractions does not increase to an absolute maximum as the intensity of the stimulus is raised. An induction shock produces a contraction or fails to do so according to its strength; if it does so at all, it produces the greatest contraction that can be produced by any strength of stimulus in the condition of the muscle at the time. From this it follows directly that the cause of the varying degrees of contraction of the heart is to be sought in changing [initial] conditions of the muscle fibres themselves. It is scarcely necessary to point out the great practical significance of this generalization.

WALTER MORLEY FLETCHER AND FREDERICK GOWLAND HOPKINS

Sir Walter Morley Fletcher and Sir Frederick Gowland Hopkins initiated modern studies on muscular metabolism. Fletcher, himself an athlete of distinction, became interested as an undergraduate at Cambridge in the problem of muscle metabolism and published at that time several important papers[12] on respiratory exchange of isolated frog muscle. With Hopkins he made a study which is now a classic upon the relation of lactic acid to muscular activity. The general conclusions reached at that time are indicated in the following passage.[13]

SURVIVAL RESPIRATION OF MUSCLE

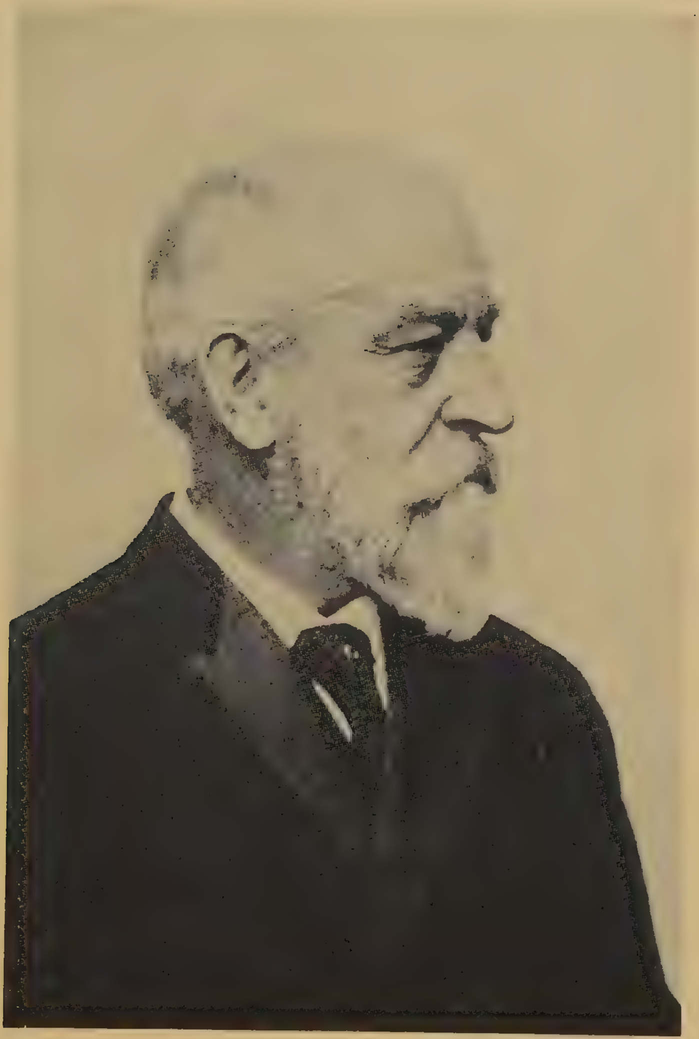
We have given proof that the survival processes in excised unstimulated muscle lead from the moment of excision onwards to a steady

---

[11] Bowditch, H. P. "Über die Eigenthümlichkeiten der Reizbarkeit, welche die Muskelfasern des Herzens zeigen." *Berichte d. Königl. Sächs. d. Ges. d. Wissen.*, 1871, Bd. 23, pp. 652-689 (p. 687).

[12] Fletcher, W. M. "The survival respiration of muscle." *Jour. Physiol.*, vol. 23, pp. 10-99, 1898; "The influence of oxygen upon the survival respiration of muscle." *Ibid.*, vol. 28, pp. 354-359; 474-498.

[13] Fletcher, W. M. and F. G. Hopkins. "Lactic acid in amphibian muscle." *Jour. Physiol.*, vol. 35, pp. 247-309, 1907 (pp. 297-298).



H. P. Bowditch

FIGURE 50. Henry Pickering Bowditch (1840-1911) (from W. B. Cannon's memoir in the *Proc. Nat. Acad.*, vol. 17, pp. 183-196, 1924).

accumulation of lactic acid, which, under most conditions, ceases entirely with loss of irritability. The increase of acid in the intact muscle is most rapid under anærobic conditions, is slower than air, and is not to be observed (at any rate for long periods after excision) in an atmosphere of pure oxygen. In the unstimulated muscle the production is, for the greater part of the survival period, very nearly proportional to the lapse of time; but stimulation produces an acceleration which may convert the curve of production velocity from a linear type into one showing exponential characters. Partial disintegration of the muscle represents a strong stimulus, inducing this acceleration to a marked degree, and a want of recognition of the rapidity of the change so induced has led many observers to ascribe much too high values to the lactic acid content of "resting" muscle. This is an error which has necessarily prevented the ascription of right values to the changes occurring during survival processes or fatigue. Exposure of the intact fibres to poisons, such as chloroform or coal gas, also accelerates the velocity of production, and, as has been shown in Part II of this paper, the action of alcohol in this respect is so marked that its uninformed use as a solvent has introduced large errors into many published estimations of lactic acid.

Our experiments make it clear that the excised but undamaged muscle when exposed to a sufficient tension of oxygen has in itself the power of dealing in some way with the lactic acid which has accumulated during fatigue. While the fibres are recovering from fatigue and regaining irritability in an atmosphere of pure oxygen, their content of lactic acid is greatly reduced. As already stated, exposure to pure oxygen also inhibits the production of the acid in fresh resting muscle. In air a slowing of the rate of production is seen, but exposure to an atmospheric tension of oxygen does not inhibit the process of formation.

There is no reason to suppose at present that an increase of oxygen tension has any influence more special than that of accelerating the penetration of the gas into the muscle mass. If, as can hardly be doubted, there occur, in the surviving tissue, processes (encouraged by anærobic conditions) which lead to acid production, opposed to others (demanding oxygen) which make, possibly, for actual inhibition of production, and, certainly, for removal after production, then it is clear that whether we shall observe an accumulation of the product or a balance, or, as a third alternative, removal of the product when formed, will depend upon the rate at which oxygen is supplied. There is every reason to believe that a sufficient tension of oxygen (not reached in air) partially restores to an excised muscle one normal asset otherwise lost on excision, a supply, namely, of the gas sufficiently rapid to turn the balance, from an accumulation to a removal, of the particular breakdown product under consideration.

LOUIS LAPICQUE

Louis Lapicque, who occupies the chair of Claude Bernard at the Sorbonne, has for the last 25 years been investigating, in collaboration with his wife, the excitatory process of irritable tissues. They have discovered a striking correlation between such properties as the rate of conduction, the speed of contraction, the latent period, etc., and the least interval of time required to produce excitation; this has shed important light upon the intimate nature of the excitatory processes, and, in addition to being of great theoretical importance, the investigations have proved to have wide application both in physiology and in clinical medicine. Prior to the work of the Lapicques, excitation had been described in vague and inexact terms; but with the introduction of 'chronaxie'—a precise and easily determined characteristic—the subject was at once clarified and quantitative methods were made possible. The following passage is taken from his paper in which the term 'chronaxie' was originally defined.[14] Though this paper was published in 1909, the work had been commenced in 1903, and hence antidates the excellent studies of Lucas published in 1907.

EXPERIMENTAL DEFINITION OF EXCITABILITY

The excitability of a tissue cannot be considered as defined when but *one* threshold of stimulation has been determined. Indeed, such an isolated determination cannot be used even in the simplest and most direct comparison, *e.g.* to discover whether excitability increases or diminishes under a given influence. Even when it has been ascertained if the stimulus originally used should be increased or diminished, the conclusion reached is only applicable to that particular stimulation and not to the general excitability of the tissue; in fact another stimulus differing from the first merely by its duration might give an entirely different, or even a contrary result.

For example, under the influence of curare, as Brücke clearly stated more than 40 years ago, the excitability of the gastrocnemius of the frog is hardly changed at all for constant currents, while it is considerably diminished for induction shocks.

To take another example: if the temperature is lowered the excitability of nerve and muscle in general is diminished for induction shocks and increased for a constant current[15]—or to put it more exactly—is diminished for brief shocks and increased for prolonged currents. If one compares the excitability of two different tissues, it is even more essential to take the time element into consideration in addition to the threshold.

---

[14] Lapicque, L. "Définition expérimentale de l'excitabilité." *Comp. Rend. Soc. Biol.* Paris, 1909, tom. 67, p. 280.

A smooth muscle which remains motionless to a violent induction shock contracts under the influence of a fairly weak constant current of several seconds duration; this constant current loses none of its force though it is of slow onset and takes a second or more to establish itself. On the other hand, the gastrocnemius of a frog which would react strongly to an induction shock or to a constant current of abrupt onset would not be affected by a much stronger constant current taking several tenths of a second to establish itself.

Is it then permissible to say that either of these muscles is *more* or *less* excitable than the other, if at the same time the method of stimulation is not indicated? The significance of the terms 'more' and 'less' changes according to the type of stimulation and they are therefore inadequate even when defining relative excitability. . . .

The best method, it seems to me, is to establish the two essential elements of excitability by two direct experimental measurements. This can be done as follows:

One must determine:

1. The intensity of a constant current of abrupt onset and prolonged duration which gives the threshold of excitability. I propose to call this intensity the *rheobase* (lowest point of current). In practice it is unnecessary to measure this intensity; if the circuit of stimulation does not need to be altered in any way it is sufficient if the voltage corresponding to that of the *rheobase* is known.

2. The duration of a constant current of abrupt onset which attains the threshold of stimulation with an intensity equal to double that of the rheobase, *i.e.* with a voltage of double that of the rheobase. I propose to call this duration the *chronaxie* (αξια, value, χρονου, of time).

This time interval is in reality characteristic of the true excitability of the tissue under consideration, and it agrees more or less with the ratio *a/b* of the hyperbolic formula; all that I have written on this subject since 1903, on my own or with Madame Lapicque, applies to it. I have proved that it (the *chronaxie*) varies, according to the tissue under consideration—not to mention the influence of temperature—from three ten-thousandths of a second (gastrocnemius of a green frog) to one second (stomach of the same animal), *i.e.,* a scale of variation of 1-3000; and it is certain that excitability exists above and below these limits.

---

[15] Gotch and Macdonald. *Journal of Physiology,* 1896. L. and M. Lapicque. *Comptes rendus de la Soc. de Biol.,* Jan. 12, 1907. Keith Lucas. *Journal of Physiology,* Dec. 31, 1907.

Determination of the time interval requisite for establishing the rheobase is necessarily inexact, since it is reached asymptomically. It equals about ten times the *chronaxie.*

Excitability is thus defined without theory or calculation by means of two experimental values.

ALEXANDER FORBES AND ALAN GREGG

Alexander Forbes and Alan Gregg of the Harvard Medical School were the earliest to make a systematic analysis of nerve impulses set up in the central nervous system and to compare them with those evoked by artificial stimulation of a peripheral nerve. It had been supposed by some physiologists that impulses arising within the brain and spinal cord differed in kind from those elicited faradically in isolated preparations, and Forbes and Gregg were the first to provide satisfactory evidence that, however elicited, nerve impulses were always of the same nature. This gave added significance to the observations of Gotch, Lucas, Adrian and others who had studied the responses of nerve trunks after removal from the body, and it proved that the all-or-none principle must be taken into account in any consideration of reflex action. In a well reasoned argument Forbes and his co-worker gave the accepted explanation of the differences between action currents of a reflex and those set up by stimulation of a motor nerve. Forbes in continuing with these investigations has given further evidence for his and Gregg's original interpretation, but the fundamental observations are contained in their first joint communication from which the following selection is made.[16]

ACTION CURRENTS OF THE FLEXION REFLEX

In general, it may be said that as compared with the direct response, the reflex action current appears after a latency of about 9σ, then rises to a maximum which is reached from four to ten times as long after its onset as is the case in the impulses directly evoked from the nerve by a single shock; and the maximum when reached is much smaller even in a maximal reflex than is evoked by maximal stimulation of the nerve.

---

[16] Forbes, A. and A. Gregg. "Electrical studies in mammalian reflexes. I. The flexion reflex." *Amer. Jour. Physiol.*, vol. 37, pp. 118-176,1915 (pp. 147, 148-149).

The more gradual rise of the electrical disturbance in the case of the reflex may be quite as easily explained in a way which harmonizes perfectly with the view that the impulse is essentially the same however evoked. It has already been suggested that we have no grounds for the conclusion that in the flexion reflex the impulses in the many neurones making up the motor nerve are discharged "in a volley" rather than in "platoon fire," to use Brücke's phrase. They might conceivably start down the nerve trunk simultaneously in all the fibres. Yet it is quite as likely, if not even probable, that the reflex times in the hundreds of separate arcs will not be exactly the same, and that the arrival of the various outgoing impulses at a given point in the nerve will be spread out over a considerable period of time. Just such a scattering in time would perfectly explain the more gradual development of the observed electrical disturbance at the point where it is recorded. It would also contribute another factor to account for the greatly reduced intensity of disturbance as compared with the direct response; for if at any given instant only a small percentage of all the fibres taking part in the reflex are at the height of their activity, at no time will there be so great a disturbance as if all were active at once. This consideration taken in connection with those already mentioned, namely, the fact that nearly half the fibres involved in the direct response are afferent and the fact that by no means all of the motor fibres are called into action by stimulation of a single afferent nerve, may well account for the smallness of the action current obtainable from the maximal reflex.

FREDERICK HAVEN PRATT

Frederick Haven Pratt, a graduate of Harvard, who occupied the Chair of Physiology at Buffalo (1912-19) and is now at Boston University, established the all-or-none principle of contraction of skeletal muscle fibres by means of direct observation. His ingenious method involved recording the movement of mercury droplets on the surface of a muscle, one fibre of which was stimulated by a pore electrode several μ in diameter. The following selection from his second paper will serve to indicate the significance of his studies.[17]

THE ALL-OR-NONE PRINCIPLE

The amount of energy transformed in muscle is characteristically far greater than that manifest in the process necessary to arouse the trans-formation. Passage from stimulus to response involves a distinct breach of continuity. A change, discrete and transitory, precedes a change revealing sources of energy relatively vast, governed in duration and intensity by no conceivable presiding extension of the original excitatory force; and yet, in skeletal muscle particularly, response is docile to behest of stimulus from its readiness to fulfil the requirements of instrumental calibration up to the marvel of emotional expression.

---

[17] Pratt, F. H. "The all-or-none principle in graded response of skeletal muscle." *Amer. Jour. Physiol.,* vol. 44, pp. 517-542, 1917 (pp. 517-518).

The determination of the general type of mechanism involved in the factor of control is plainly fundamental to the whole conception of the energetics of muscle. That a minimal stimulus should be capable of awakening the massive charge of an unstable system, and at once restoring equilibrium in relative accordance with its own subtle measure of intensity, is a conception fraught with an assumption of organic complexity unique in its nature, and one which places the problem of muscle contraction in a hazardous field. If, on the contrary, the mechanism of control be regarded as discontinuous with the responding system, conceding to the latter an inherent, determinate capacity for energy release, it is possible to reinstate the control factor as a mechanism for simply utilizing multiples of energy yielding elements. The excitatory process, in accordance with its access to one or more systems of definite dynamic capacity, will then discharge one or more in strict relation to that access; that is, in strict relation to its own demands.

The alternatives present so great a divergence, on the score of both nature and complexity of mechanism, that the acceptance of one or the other must determine widely different interpretations of contractile phenomenon—gross, microscopic and physico-chemical. For in one case we must recognize the events in sequence as follows:

Excitation—/initiation of discharge in responding system—/limitation of magnitude of discharge (massive) in strict conformity to magnitude of excitation (relatively meagre); and in the other.

Excitation—/full discharge in every responding system to which the excitatory influence has effective access.

Thus the first alternative involves, in the same system, initiative plus limitation; the second, initiative without limitation in all systems excited. In the first, control necessitates an inhibition of discharge, quantitavely selective, in a disturbed unstable system; in the second, it requires only that excitation penetrate to each quantum of energy needed in the response.

ARCHIBALD VIVIAN HILL AND WILLIAM HARTREE

ARCHIBALD VIVIAN HILL and WILLIAM HARTREE have contributed extensively to knowledge of the thermodynamics of muscle and have been largely responsible for the modern conception of muscle metabolism. In the course of their fruitful collaboration they have studied from the point of view of the physical chemist, not only the reactions of isolated muscle, but also the performance of the intact human organism. The analysis of heat-production of isolated muscle has been made possible through constant improvements in instruments for detecting all thermal changes. The separation of heat-production into four distinct phases, correlated with corresponding phases of mechanical activity, represents perhaps this most important discovery. The following extract has been taken from their original paper describing this result.[18]

THE FOUR PHASES OF HEAT-PRODUCTION OF MUSCLE

When a muscle is stimulated isometrically it passes gradually into a new elastic condition: as stimulation is continued the elastic condition continues to change up to a certain limit, after which it remains constant; when stimulation ends, the muscle reverts gradually to its original elastic state. Expressed in another way the muscle, on excitation, gradually develops elastic potential energy: as the excitation proceeds this potential energy reaches a constant value; when the excitation ends the potential energy disappears. Finally, in the presence of oxygen there occur certain recovery processes accompanied by an evolution of heat and restoring the muscle to its previous internal condition. These four stages, viz. the development of the mechanical response, its maintenance and its disappearance, followed by the oxidative recovery from activity, will be referred to below as the four phases of muscular contraction. The questions arise "how much of the total heat-production is to be associated with each phase and how is it distributed in time?" The experiments described in this paper represent an attempt to answer this question. The investigation arose originally from the simpler question, "what happens to the potential energy of a muscle excited isometrically, when the muscle relaxes?" There are clearly two possible answers: (i) that the potential energy, if not utilised in doing work, is re-absorbed more or less reversibly by the muscle for use in a subsequent contraction; or (ii) that it is degraded into heat by processes analogous (say) to leakage, diffusion or neutralisation. The experiments have decided in favour of the second alternative. . . . .

---

[18] Hill, A. V. and Hartree, W. "The four phases of heat-production of muscle." *Jour. Physiol.*, vol. 54, pp. 84-128, 1929, (pp. 84-85, 106-107, 126-127).

2. EXPERIMENTAL RESULTS

The present part of this paper deals only with the heat produced during the first few seconds after excitation and is confined to the case of tetanic stimulation, for periods of 0.1 to 6.0 seconds, of the sartorius muscles of the frog (Rana temp.). It is clearly desirable to repeat the investigation on other and more slowly moving muscles and we hope to do this later. The experiments have been carried out at various temperatures, in oxygen and in nitrogen, and under various conditions of fatigue.

The first important point brought out by these experiments is that, provided that advanced fatigue be avoided, no difference can be discerned in the initial stages of the heat-production between muscles kept in oxygen and muscles left for a long time in nitrogen. It is known, and in experiments performed recently we have amply confirmed, that in the later stages there is considerable difference in the heat-production according as the muscles are kept in oxygen or nitrogen; this difference is attributed to slow oxidative recovery processes possible (at least to their full extent) only in the presence of oxygen by which the muscle is restored in some manner to its previous condition.

Oxygen however has no effect whatever on the *initial* heat-production. It is not necessary to give all the evidence in detail as it is negative in kind and we will include below only an account of one experiment devoted specifically to testing this point. The direct comparison of the curves made by the muscle (a) in oxygen and (b) in nitrogen is an extremely sensitive one, as no analysis of the records is required in order to allow us to assert that the two curves are the same; thus any possible error in the analysis is eliminated. Great care was taken in the nitrogen experiments to eliminate the oxygen completely by sweeping it out as far as possible with boiled Ringer's solution in which the muscles were allowed to rest for some time, then leaving the muscles for some time in nitrogen before making an observation, and lastly giving them (in most cases) a few preliminary stimuli in order to assist them to use up any traces of dissolved oxygen. A mild degree of exercise not leading to appreciable fatigue does not appear to alter the type of the thermal response: advanced fatigue however does change it by diminishing the relative amount of heat liberated in the processes of relaxation. Muscles kept in nitrogen are readily fatigued and it is necessary therefore to avoid over-stimulating them. . . . .

In a prolonged contraction (*e.g.* 2 secs. tetanus) of the sartorius, the heat production may be resolved into the following four phases: (a) an initial rapid production, diminishing gradually in rate as the stimulus proceeds; (b) a smaller constant heat-production maintained so long as the stimulus is maintained, and ending shortly after the stimulus ceases; (c) a relatively large evolution of heat, occurring rather suddenly during the later stages of relaxation; and (d) a large, but slow, production of heat occurring in the presence of oxygen for some minutes after the contraction is over.

In the twitch evoked by a single shock or by a very short tetanus only three of these phases occur, (a), (c) and (d). It is natural to associate (a) with the development, (b) with the maintenance and (c) with the disappearance of the mechanical response, and to connect (d) with the processes of recovery. It is probable that the heat produced during relaxation is derived from the mechanical potential energy developed on excitation, and lost in relaxation.

The interval between the second and third phases of the initial heat-production depends largely on the temperature. In a short twitch at 0° C. it is of the order of 0.7 sec.: at 25° C. it is too short to be measured directly with the instruments at present employed. All the more reliable experiments have been performed at a low temperature.

GENICHI KATO

GENICHI KATO, the Professor of Physiology at Keio University, Tokyo, is by common consent the leader of the great school of physiology in Japan. He has recently placed physiologists in his debt through a series of important experiments upon the effect of narcotics on peripheral nerve. Taking advantage of the enormous species of frog common in Japan he has been able to secure long stretches of nerve which could be subjected to the action of a narcotic. His experiments are beautifully conceived and have that simplicity and directness which make them appealing and convincing to a degree seldom felt of observations in this special field of work. He has thrown important light upon the nature of conduction in peripheral nerve and now, largely as a result of his investigations, it is possible to adopt a satisfactory hypothesis concerning the nature of the nerve impulse.[19]

[19] Kato, G. *The theory of decrementless conduction in narcotised region of nerve.* Tokyo: Nankodo, v+166 pp., 6 plates, 1924 (pp. 1; 11; 13; 14-18). See also *The further studies on decrementless conduction.* Tokyo: Nankodo, viii+163 pp., 1926.

DECREMENTLESS CONDUCTION

My "theory of decrementless conduction" of nervous impulse in narcotised region of nerve was first brought to publication at the second general meeting of the Japanese Physiological Society which was held in April, 1923, at Kyushu Imperial University in Fukuoka, and secondly in November of the same year it was delivered as a special lecture at the fourth general meeting of the Keio Medical Society, Tokyo. I have rewritten this lecture to form the present monograph.

In the experiments we have used principally the male species of the large healthy Japanese toads, Bufo vulgaris Japonicus, which often weigh as heavy as about 350 gram., and from them we made nerve-muscle preparations, sciatic-gastrocnemius, the nerve of which was, as a rule, not shorter than 10 centimeters. This extraordinary large toad facilitated us to expose so long a stretch of nerve as eight centimeters to the action of narcotics.

INFLUENCE OF THE LENGTH OF NARCOTISED NERVE ON THE DEPTH OF NARCOSIS REQUIRED TO ABOLISH CONDUCTION

I Preliminary Test

As it was stated in the foregoing chapter, the firing of a train of gunpowder closely resembles to the conduction of nervous impulse. The combustion of gunpowder, however, takes place too instantaneously to observe the mode of progression closely. So Dr. Maki took a Japanese incense, a stick of slowly combusting substance, as a model of nerve. Attention was at first attracted to the rate of conduction: After he had tested that the combustion propagated along an "incense" with a slow but constant rate, he immersed the both ends (AB, CD) of it in a saturated $KCLO_3$ solution and dried. Let us suppose the part BC, free from $KCLO_3$, as a stretch of nerve that is narcotised. The combustion propagated with a constant rate along the "incense" so treated from A to B but more rapidly than before and from B to C with reduced but constant (not progressively reduced) rate and from C to D as rapidly as in between A and B. The reduction of the rate of progression in the region BC occurred at once in the immediate neighbourhood of B and no further reduction was observed along its course. Thus, no decrement in the rate of conduction!

MAIN TEST

The most important experiment upon which "decrement theory" has been based is, as mentioned before, that the time required to abolish conduction becomes gradually less as the length of nerve to be narcotised is made greater.

I suggested, therefore, to Dr. Maki that he should make experiments on this line, and special precautions were taken in following points:

1. that two sciatic-gastrocnemius preparations were taken from the same toad and the different lengths of these two nerves were narcotised and the times required to suspend conduction from "outside electrodes" A and A′ were determined with fully maximal stimulus and they were compared with each other, and the comparison was never made between those from different toads or frogs.
2. that the nerves were exposed to narcotic simultaneously in the same narcotising chamber, so that the different lengths of the two nerves taken from the same toad could be exposed to the action of narcotic in the same condition.
3. that special cares were taken in making nerve-muscle preparation as well as in setting it up in narcotising chamber. To avoid inequality of the action of narcotic in any part of the nerve, all the nervous branches were ligated as far as possible from the main trunk.

Before we proceed further to compare the times required to abolish conduction in different lengths of narcotised nerves, we must stop a moment to determine experimentally to what extent the times necessary for extinction of conduction in the same length of two narcotised nerves coincide.

A. *The extent of diversity of the times required to abolish conduction in the same length of two narcotised nerves.*

Under the precaution mentioned above, Dr. Maki has determined the times required to abolish conduction in the same length of nerves taken from the same toad. The differences of the times so determined are given as % of the time for B. In some cases the times were the same for both A and B but it was not a matter of usual occurrence. Some diversity was found in most of the cases, the maximum diversity being as large as twenty percent, though such a difference occurs very rarely.

B. *The times required to suspend conduction in the different lengths of narcotised nerves.*

In the narcotising chamber specified in the precautions different lengths of two nerves taken from the same toad were exposed simultaneously to the action of ether vapour. By regulating the rate of bubbling of ether vapour, the concentration of the narcotic, to which the nerves were exposed, was changed in every experiment, so that the comparison could be made in the wide range of times. In No. 5 the conduction abolished within 7 minutes, while in No. 15 it lasted as long as about 80 minutes. As I have mentioned before, the comparison should be made only between the times given in the same number of experiments (these were determined in two nerves taken from the same toad).

The diversity of the times are given as % of the time determined in the shorter region of narcotised nerve, indicates a case in which the conduction abolished earlier in longer region of nerve, as previous investigators have informed, while — indicates a case, in which the conduction was suspended earlier in the shorter narcotised region. In No. 3 it will be seen that the times determined were practically the same both in short and long narcotised regions, the conduction being suspended in the shorter region one second earlier. In the other cases the differences oscillated equally on both sides and there could be seen no tendency that the conduction would be abolished earlier in the longer stretch of narcotised nerve. If it be true that the longer is the narcotised region, the shorter is the time for abolition of conduction, then there must be a marked difference of times in No. 19, 20 and 21 in which the lengths of the nerves narcotised were in such a ratio as 11.4 to 1.8. It must, therefore, be concluded that the length of narcotised nerve has no influence at all on the depth of narcosis required to abolish conduction. [The same result was also obtained using as narcotics chloroform, alcohol, urethane, chloral-hydrate and cocaine.]

ETHER AS A NARCOTIC

No.	Time for longer region	cm.	Time for shorter region	cm.	%
1	15′ 10″	3.5	15′ 0″	2.5	—1.11
2	18′ 20″	3.5	18′ 25″	2.5	+0.45
3	22′ 35″	3.5	22′ 34″	2.5	—0.07
15	80′ 9″	3.5	82′ 18″	1.8	+2.65
19	58′ 13″	11.5	45′ 36″	1.8	—6.62
20	19′ 33″	11.5	18′ 32″	1.8	—5.49
21	11′ 10″	11.5	12′ 0″	1.8	+6.94

JOSEPH ERLANGER AND HERBERT S. GASSER

Joseph Erlanger and Herbert S. Gasser of Washington University Medical School, St. Louis, became engaged in 1921 in a joint investigation which, since that time, has completely revolutionized knowledge concerning conduction in peripheral nerve. Through application of the principle of valve amplification and the use of an inertialess recording system (cathode ray oscillograph), they have been able to detect in a mixed nerve, action currents of fibres subserving different functions. The correlation of rate of conduction with fibre diameter, in itself an important contribution, is overshadowed by their recent allocation of function to the various waves in their action current records. The following selection is taken from one of their early papers.[20]

Discussion and crucial experiment. Turning now to a consideration of the nature of the waves of the compound action current, the evidence we have thus far presented is so clearly in favor of their being discrete action currents originating simultaneously under the stimulating electrode and traveling along the nerve at different rates, that no other plausible way of accounting for them seems possible. In our preliminary statement, published before this evidence had become so convincing, other possibilities were mentioned, but even at that stage of the investigation these were easily disposed of. The waves cannot, for instance, be due to strong stimulation because they are not evident in the phrenic nerve under any circumstances. For the same reason they cannot, be attributed to the development of discrete, regular, decremental states resulting from injury to the nerve in preparation. As a matter of fact injuring the phrenic nerve by manipulating it roughly, or by painting it with scalding water, or with 95 per cent alcohol, does not cause waves to appear in its action current.

The phrenic differs from the sciatic nerve in that branches in the former are insignificant, but constitute a striking feature of the latter. The advisability of ascertaining whether the branches have anything to do with the waved nature of the action current in the sciatic nerve became apparent during the course of some experiments that have recently been performed. In these experiments it has been found that when an inert conductor, such for example, as an idle non-polarizable

[20] Erlanger, J. and H. S. Gasser. "The compound nature of the action current of nerve as disclosed by the cathode ray oscillograph." *Amer. Jour. Physiol.*, vol. 70, pp. 624-666, 1924 (pp. 659-660; 662-663; 665).

electrode, rests upon the nerve anywhere *between* the leads, the action current is deformed by a notch or by a wave in a manner to be described elsewhere. Not only is this deformation produced by a foreign conductor, but also by the stumps of the nerve's own branches. It has, however, been found that the waves with which the present paper concerns itself are not due to the presence of branches. The waves appear when there are no stumps between leads; indeed they have been obtained when the preparation has consisted only of the part of a very large bull frog's sciatic nerve that is entirely free of branches.

The waves then represent discrete action currents in different nerve fibers. In the present state of our knowledge it is, however, impossible to assign to the waves definite functions; and speculation on this phase of the subject based on the results we have thus far accumulated has failed as yet to suggest even a satisfactory working hypothesis. To be sure it is not at all surprising in view of the varied histological composition of mixed nerves to find that the action current of such a nerve as the sciatic is compound. Indeed the varied histological composition of nerve has led Langley recently to venture the opinion "that the size" for instance "of the fibers has some definite connection with the kind of tissue in which the fiber ends." Now that the action current of a mixed nerve has been found to be compound one would naturally be inclined to infer that each component is concerned with the mediation of some particular type of response. For a clue to the solution of the problem one would naturally turn first to the two great groups of fibers of the peripheral nervous system, namely, motor and sensory. It is, however, currently believed that the conduction rate of the action current is of the same order of magnitude in afferent and efferent fibers. The fact that thus far we have observed only two waves in the action current of the saphenous nerve (dog) whereas the action current of the tibial nerve dissociates into three, sometimes into four, waves, would naturally lead one to attribute this difference to the absence of voluntary motor fibers in the former nerve. But this possibility seems to be precluded by our data in that they show that the leading wave both in the saphenous and in the sciatic action currents has essentially the same rate of conduction. That motor and sensory fibers of a mixed nerve have discrete action currents traveling at different rates is negatived also by the form of the action current in the phrenic nerve. Despite the fact that this nerve contains, in addition to motor fibers "an abundance of fibers from sensory ganglia" its action current has always been simple in form.

Differences in the nature of nerve impulses on the afferent side have been invoked by Head and collaborators, if we read these authors aright, in order to account for the regrouping of somatic impressions which they describe as occurring within the central nervous system. "Each end organ in the skin," they write, "is capable of reacting to the mass stimulation of the environment in a specific manner . . . When these *peculiar impulses* (italics ours) reach the spinal cord, they are discharged into secondary systems, each of which is guarded by specific receptors . . . It is as if the gallery of a concert hall were fitted with a series of resonators, each of which was tuned to a certain note." The indications we have obtained of differences in the properties of groups of fibers composing a nerve supply an experimental basis for the "peculiar impulses" which Head and Thompson find it necessary to predicate in order to account for their clinical observations. Granting the existence of peculiar impulses in particular nerve fibers, the only further condition that would be needed to effect a regrouping of somatic impulses is that the secondary systems, in the sense of Head and Thompson, respond most readily, as do the peripheral receptors, to their adequate stimuli.

These few examples will suffice to indicate the possible applications of our finding that the fibers composing a mixed nerve are not all alike in a physiological sense. To repeat, these differences may mean that the stimuli the fibers deliver are different and perhaps adequate to the structures they innervate. It should be made clear, however, that we have not yet succeeded in obtaining any experimental evidence that can be regarded as proving the existence of differences in the stimulating values of the impulses delivered by the different types of fibers. The results of our investigations do, however, prove that in certain of the mixed nerves the action current is compound. Furthermore they indicate the possibility, which is being investigated further, that each of the potential waves of any action current is a composite of potential changes slightly out of phase in individual nerve fibers. However this may be, we suggest for the sake of convenience that action currents from which discrete waves separate out be called *compound* and that the potential waves which lengthen on propagation be designated *simple* action currents.

EDGAR DOUGLAS ADRIAN AND YNGVE ZOTTERMAN

Edgar Douglas Adrian and Yngve Zotterman recorded in 1926 a series of remarkable observations[21] upon the responses of single sensory end-organs to a natural stimulus (tension) on the basis of which they were led to formulate their important conception of "adaptation" of receptors to stimuli. Their prediction that a similar process of adaptation would be found in other units of the nervous system has been amply justified by recent work, and the theory has already begun to assume an importance comparable with Müller's law of specific nerve energies.

NATURE OF ADAPTATION

The gradual decline in rhythm which occurs with a steady stimulus has already been described, but its cause has not been dealt with. It might be due to a gradual decrease in the excitability of the end-organs or to a gradual increase in their refractory period, or to both these causes. If only the former were in action, the effective value of the stimulus would decrease so that longer and longer intervals would have to elapse after each impulse before the end-organ had reached the degree of excitability necessary for the setting up of a fresh impulse. A slowing of the rate of recovery would have the same effect, although the excitability remained unaltered. When a gradually increasing current is applied to a nerve fibre the adaptation which occurs is confined to the mechanism of excitation, for the stimulus may fail to set up an impulse at all if it increases too slowly. Presumably by the failure of a constant current to set up more than one impulse is due to the same cause, *i.e.* to the rapid decline in the stimulating value of the current. The rate of recovery may be altered in the region which becomes adapted, and Brücke has shown that the refractory period of the nerve fibre or nerve ending becomes prolonged when a rapid succession of impulses are passing, but this by itself would not account for the complete failure to set up a second impulse. So, if the decline in rhythm from the end-organ is due to a process of adaptation of the same kind as that occurring in the nerve fibre we should expect to find evidence of a change in excitability with or without a change in refractory period in addition.

---

[21] Adrian, E. G. and Zotterman, Y. "The impulses produced by sensory nerve-endings. Part 2. The response of a Single End-Organ." *Jour. Physiol.,* vol. 61, pp. 151-171, 1926 (pp. 167-170).

In order to study the process more thoroughly we have increased the tension on the muscle at varying rates, recording both the tension on the muscle at each moment and the frequency of the afferent impulses. The tension was applied by a short lever fixed in the centre of a twisted elastic band. A similar lever at one end of the band was rotated at varying speeds through a known angle and its movement was communicated to a pointer moving across the slit of the film camera. The lever in the middle of the band is fixed to the thread from the muscle and can only move through a very small arc, but when the end lever is rotated the tension on the thread is increased and its final value depends on the amount of movement of the end lever. The tension developed for different movements of the end lever was determined by hanging weights on the centre lever and finding the amount of movement required to raise them. . . . With very rapid loading the maximum frequency is reached at about the same moment as the maximum tension, but with more gradual loading the maximum frequency is much less and it is reached some time before the stimulus is at its full value. These curves would be the natural result of any process of adaptation and they merely serve to emphasize the fact that the adaptation begins at the moment that the stimulus is applied. A more significant fact is shown in Fig. 10 B, which records also the effects of a rapid unloading after the tension had been at its full value for 17 seconds. In all our experiments the result of this has been a complete cessation of all impulses for a period varying from .75 to 1.5 sec. followed by a gradual return to the normal "resting" frequency of 3-8 per second. It is difficult to explain this pause in the discharges without supposing that a true fall of excitability has occurred. During the period of stimulation the frequency has fallen to about half its initial value. If this fall is due to an increase in the refractory period the latter must have risen to about double its initial value, and we should expect to find a discharge at half the initial resting frequency when the stimulus is removed. Actually the initial frequency is 6 per second but there is a pause of 1.3 sec. at the end of stimulation.

We conclude that the decline in the frequency of response is due in part at least to a fall of excitability in the end-organs when the stimulus is continued and their adaptation is thus brought into line with the much more rapid process which occurs in the nerve fibre.

Remarks

The behaviour of the end-organs which we have examined seems to be explained very simply in terms of the general properties of excitable tissues, in particular by the phenomena of adaptation and of the refractory state. It is probable, therefore, that other types of end-organ will be found to react in much the same way to the particular stimuli which call them into play. This probability is strengthened by the close resemblance of the records of impulses in various types of sensory nerve dealt with in Part I, though an investigation of other single end-organs will be needed to establish it. A point of considerable interest is that the frequency of the discharge from the end-organ is so much slower than the maximum frequency which the nerve fibre can tolerate. If this is true of end-organs in general it means that the frequency of the impulses in the fibres of the auditory and of the optic nerves is lower than is often supposed. This again must wait for experimental confirmation. Finally, it is worth enquiring whether the synapses of the central nervous system may not sometimes react in the same way as the end-organ to the mass of impulses reaching them.

CHAPTER VII

THE CENTRAL NERVOUS SYSTEM

K*NOWLEDGE* of the nervous system has developed to a large extent independently of other branches of physiological thought, for, unlike these, it has drawn but little upon the laws of physics and chemistry. In the early days the nervous system proved difficult of approach, not only because of the obscurity surrounding activities of its individual units, but rather on account of its complexity of structure. Even in the eighteenth century physiologists had grasped many of the fundamental facts relating to conduction in nerve trunks, but it is only in modern times that the problem of structure has been effectively met, largely, it may be said, through the introduction of the conception of integration; for it is the theory of the integrative action of the nervous system that has made possible an intelligent experimental analysis of its functions in terms of its overwhelming structural complexity.

The conception of reflex action formed the beginning of the modern interpretation. Descartes dimly grasped the notion without fully appreciating the significance of his speculation. Hales and Stuart found that decapitated frogs ceased moving when the spinal cord was destroyed, but it remained for Robert Whytt to define reflex action with adequate experimental justification for his conclusions. Prochaska generalised the conception without, however, offering much significant experimental data. From the controversy of Bell and Magendie there emerged, largely through the genius of Magendie, the fact that incoming and outgoing pathways of the nervous system are separate morphological entities. Herbert Mayo then proved that a small segment of the nervous system might be sufficient for the maintenance of a reflex, and Marshall Hall soon after began to teach that the spinal cord is in reality a series of interrelated segments, each with its own circumscribed reflex arcs. When reflex action had been firmly established, investigators next attempted to analyse the functions of individual regions of the nervous system. Rolando and Flourens approached the cerebellum; Fritsch and Hitzig defined the motor area; and David Ferrier, with the clinical stimulus constantly before him, gave the rational explanation of hemiplegia and hemianopsia, and in so doing *localised* for the first time the more important functions of the cerebral hemispheres. The theory of reflex integration, which is associated with the name of Sherrington, has clarified the bewildering mass of clinical and physiological data concerning the various levels of function in the nervous system which had been accumulating since the time of Hughlings Jackson.

RENÉ DESCARTES

René Descartes (1596-1650), the philosopher, took the functions of living organisms into the sphere of his speculations and wrote what is sometimes erroneously described as the first European text-book of physiology.[1] Since he was not an experimentalist, the cold logic of the experimental method had little appeal to his speculative turn of mind. He regarded the human body as a machine directed by the "rational soul" which dwelt in the pineal gland, and he dimly grasped the conception of reflex action, as the following paragraph will indicate; but with Descartes the conception was an *ad hoc* assumption unaccompanied by any experimental justification.[2] The same is true of his interesting description of reciprocal innervation of the eye muscles, also given below.

L'ÂME RAISONNABLE

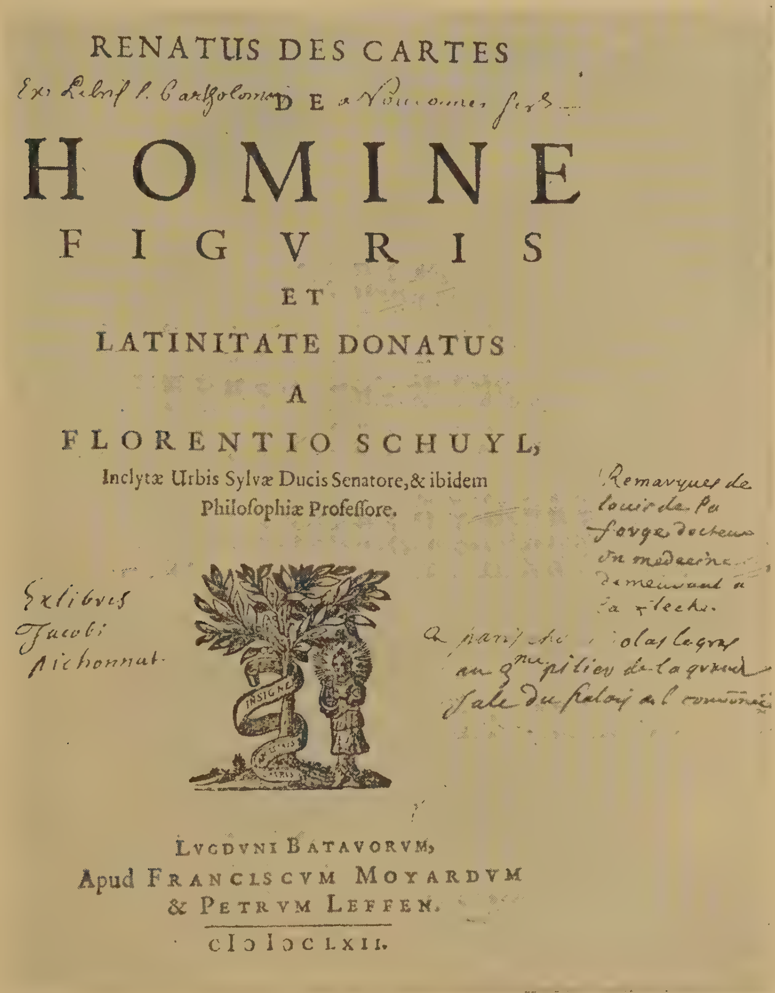
The animal spirits resemble a very subtle fluid, or rather a very pure and lively flame, and are continually generated in the heart, and ascend to the brain as to a sort of reservoir. Hence they pass into the nerves and are distributed to the muscles, causing contraction, or relaxation, according to their quantity.

In proportion as the animal spirits enter the cavities of the brain, they pass thence into the pores of its substance, and from these pores into the nerves; where according as they enter, or even only tend to enter, more or less, into this or that nerve, they have the power of changing the shape of the muscles into which the nerves are inserted, and by this means making all the limbs move. Thus, as you may have seen in the grottoes and fountains in our gardens, the force with which the water issues from its reservoir is sufficient to put into motion various machines, and even to make them play several instruments, or pronounce words, according to the varied disposition of the tubes which conduct

---

[1] The first textbook of physiology was that of Walter Charleton which appeared in London in 1659, and bore the title *Natural history of nutrition, life and voluntary motion. Containing all the new discoveries of anatomists', and most probable opinions of physicians, concerning the œconomie of human nature; methodically delivered in exercitations physico-anatomical,* London: Henry Herringman, 210 pp., 7 leaves, 8°, 1659. Charleton deserves credit for having appreciated at a very early date the significance of the experimental method, although he himself can scarcely be recognized as an ardent exponent.

[2] Descartres, R. *De homine figuris et latinitate donatus a Florentio Schuyl.* Leyden: Leffen and Franciscum Moyardum, [34] + 121 + [8] + 85 pp. + 1 l., 6 plates, 1662. The phrase "latinitate donatus" indicates that the manuscript was originally in French. The French text, however, was not published until 1664. The original figures showing the valves of the heart and the diagrams of the pineal gland appear only in the first two Latin editions of 1662 and 1664. In subsequent editions the diagrams were redrawn by Louis de La Forge, the French editor, and many of them are scarcely recognizable when compared with the originals from which they were taken.



RENATUS DES CARTES
Ex Libris P. Bartholomei [illegible]
DE
HOMINE
FIGVRIS
ET
LATINITATE DONATUS
A
FLORENTIO SCHUYL,
Inclytæ Urbis Sylvæ Ducis Senatore, & ibidem
Philoſophiæ Profeſſore.

Ex libris
Jacobi
Pichonnat.

Remarques de
louis de la
forge docteur
en medecine,
demeurant a
la flèche.

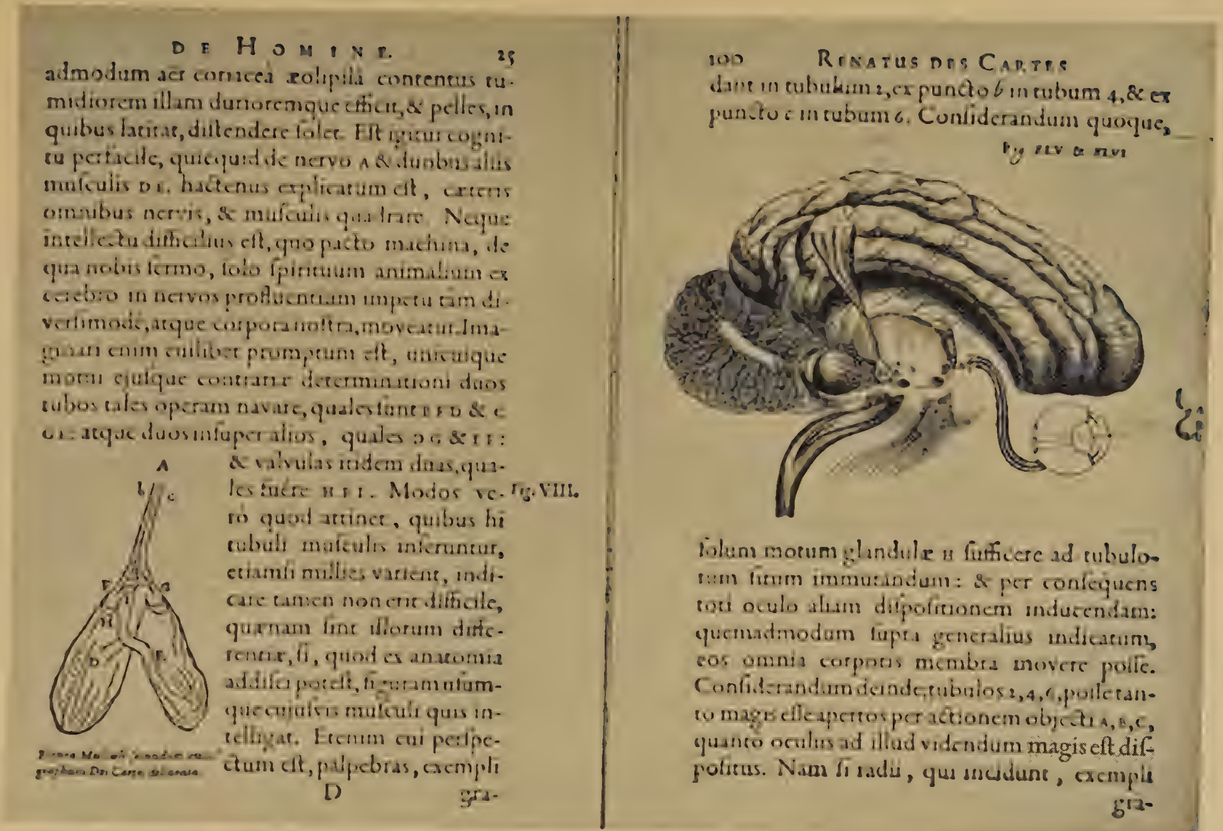
A paris chez [illegible] Nicolas le gras
au 3me pilier de la grande
salle du palais a l' [illegible]

LVGDVNI BATAVORVM,
Apud FRANCISCVM MOYARDVM
& PETRVM LEFFEN.
CIƆ IƆ C LXII.

FIGURE 51. The title-page of the first edition of Descartes' *De homine,* 1662, which contains the passages on reflex action, reciprocal innervation and the pineal gland as the seat of the soul.

the water. Indeed, the nerves of the machine may very well be compared with the tubes of these waterworks; its muscles and tendons with the other various engines and springs which seem to move these machines; its animal spirits to the water which impels them, of which the heart is the source or fountain; while the cavities of the brain are the central reservoir. Moreover, breathing and other like acts which are as natural and usual to the body or machine, and which depend on the flow of the spirits, are like the movements of a clock, or of a mill, which may be kept going by the ordinary flow of water. External objects which, by their mere presence, act upon the organs of sense; and which, by this means, determine the machine to move in many different ways, according as the parts of the brain of the machine are arranged, may be compared to the strangers who, entering into one of the grottoes of these waterworks, unconsciously themselves cause the movements which they witness. For they cannot enter without treading upon certain planks which are so disposed that, if they approach a bathing Diana, they cause her to hide among the reeds; and if they attempt to follow her, they see approaching towards them a Neptune, who threatens them with his trident; or if they pass in another direction they cause some sea-monster to dart out who vomits water into their faces; or like contrivances, according to the fancy of the engineers who made them. And lastly, when the rational soul—*l'âme raisonnable*—is lodged in this machine, it will have its principal seat in the brain, and will take the place of the engineer or 'fountaineer', who ought to be in that part of the works or reservoir with which all the various tubes are connected, when he wishes to quicken or to slacken, or in any way to alter their movements.

[The final summary is as follows]: I desire you to consider all the functions which I have attributed to this machine [the body], as the digestion of food, the pulsation of the heart and of the arteries; the nutrition and the growth of the limbs; respiration, wakefulness, and sleep; the reception of light, sounds, odours, flavours, heat, and suchlike qualities, in the organs of the external senses; the impression of the ideas of these in the organ of common sense and in the imagination; the retention, or the impression, of these ideas on the memory; the internal movements of the appetites and the passions; and lastly, the external movements of all the limbs, which follow so aptly, as well as the action of the objects which are presented to the senses, as the impressions which meet in the memory, that they imitate as nearly as possible



DE HOMINE. 25

admodum aer corneâ æolipilâ contentus tumidiorem illam durioremque efficit, & pelles, in quibus latitat, diſtendere ſolet. Eſt igitur cognitu perfacile, quicquid de nervo A & duobus aliis muſculis D E, hactenus explicatum eſt, cæteris omnibus nervis, & muſculis quadrare. Neque intellectu difficilius eſt, quo pacto machina, de qua nobis ſermo, ſolo ſpirituum animalium ex cerebro in nervos profluentium impetu tam diverſimodè, atque corpora noſtra, moveatur. Imaginari enim cuilibet promptum eſt, unicuique motui ejuſque contrariæ determinationi duos tubos tales operam navare, quales ſunt B F D & C G E: atque duos inſuper alios, quales D G & E F: & valvulas itidem duas, quales fuere H & I. Modos verò quod attinet, quibus hi tubuli muſculis inſeruntur, etiamſi millies varient, indicare tamen non erit difficile, quænam ſint illorum differentiæ, ſi, quod ex anatomia addiſci poteſt, figuram utriuſque cujuſvis muſculi quis intelligat. Etenim cui perſpectum eſt, palpebras, exempli gra-

Fig. VIII.

D

100 RENATUS DES CARTES

dare in tubulum 2, ex puncto *b* in tubum 4, & ex puncto *c* in tubum 6. Conſiderandum quoque,

Fig. XLV & XLVI

ſolum motum glandulæ H ſufficere ad tubulorum ſitum immutandum: & per conſequens toti oculo aliam diſpoſitionem inducendam: quemadmodum ſupra generalius indicatum, eos omnia corporis membra movere poſſe. Conſiderandum deinde, tubulos 2, 4, 6, poſſe tanto magis eſſe apertos per actionem objecti A, B, C, quanto oculus ad illud videndum magis eſt diſpoſitus. Nam ſi radii, qui incidunt, exempli gra-

FIGURE 52 A Descartes' original diagrams illustrating reciprocal innervation of the eye muscles B. One of Descartes' diagrams illustrating the effect of light upon the rational soul lying within the pineal

those of a real man; I desire, I say, that you should consider that these functions in this machine naturally proceed from the mere arrangement of its organs, neither more, nor less than do the movements of a clock, or other automaton, from that of its weights and wheels; so that so far as these are concerned, it is unnecessary to conceive in it any soul—whether vegetative or sensitive—or any other principle of motion, or of life, than its blood and its spirits agitated by the heat of the fire which burns continually in its heart, and which is in no wise essentially different in nature from all the fires which are met with in inanimate bodies.

RECIPROCAL INNERVATION OF THE EYE MUSCLES

Let us imagine a tube or small nerve, bf, flowing into the muscle D—which I am supposing is one of those which move the eye, and there dividing into several branches, loose in texture, which stretch or shrink according to the quantity of animal spirits which flow in or out of them, and whose ramifications are so arranged that the animal spirits flowing into them cause the whole body of the muscle to swell and shorten, thus pulling the eye to which it is attached towards it; on the other hand when the animal spirits flow out of the muscle it shrinks and lengthens.

Besides bf, there is another tube, ef, through which the animal spirits flow into muscle D, and there is yet another tube, dg, by which they flow out of it. Muscle E, which I assume moves the eye in the opposite direction to muscle D, receives the animal spirits from the brain through the tube cg, while those from muscle D flow through dg to E, which returns them to D by ef. There is no visible exit for the spirits contained in muscles D and E, and apparently they can only flow from one muscle to another, but these spirits are composed of such minute particles, which become even smaller owing to their ceaseless motion, that they are continually escaping through the surface and flesh of the muscles, while more are always flowing in by the two tubes, bf, and cg.

There is a small membrane, Hfi, separating the tubes bf and ef and acting as a kind of door. It has two angles, H and I, so arranged that when the animal spirits which tend to flow down from b towards H are stronger than those which are flowing up from e to i, the former push down this membrane, thus making an opening through which the latter can come through and join them as they flow towards muscle D; but when the spirits flowing up from e to i are stronger, or even as strong, as the others, they raise the membrane Hfi so that it remains closed, thus barring their own exit from muscle E; while if there is not sufficient force on either side to push against Hfi, it normally remains half-open. If, as sometimes happens, the spirits in muscle D tend to flow out through dfe or dfb, the fold H can swell out and block their passage. Between cg and dg there is another small membrane or valvule g, similar to Hfi, which normally remains half-open, and which can be closed by the spirits flowing from dg and opened by those flowing from cg.

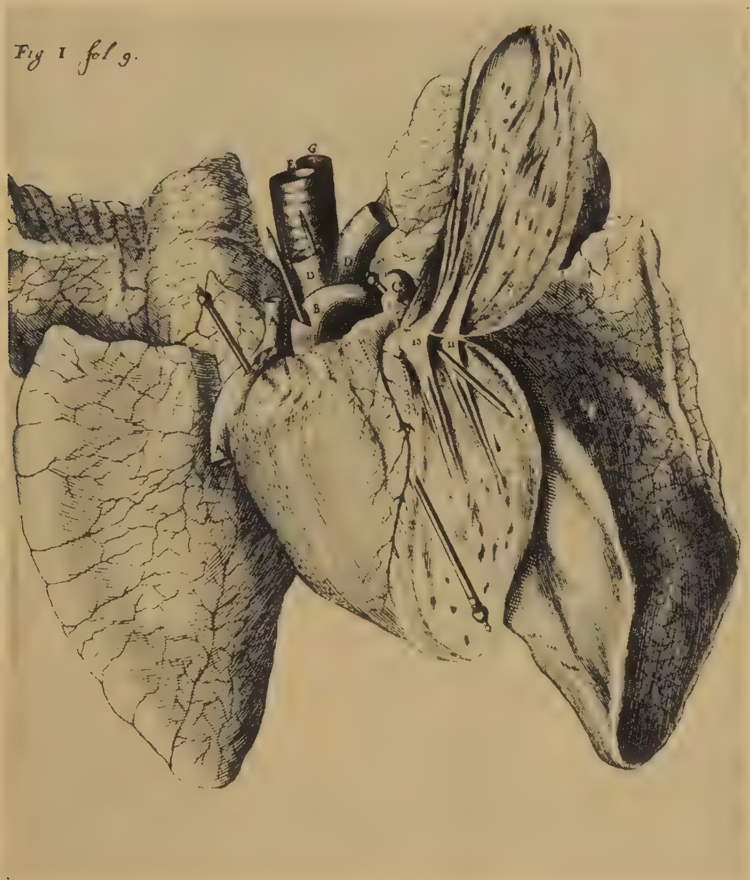


FIGURE 53. Descartes' excellent figure of the heart with one of the flaps up showing the corda tendinae. This is one of the earliest instances of the use of superimposed drawings to illustrate successive anatomical layers.

From all this it follows naturally that when the animal spirits in the brain do not tend, or hardly tend at all, to flow through the tubes, bf, cg, the two valvules f and g remain half-open and they and the muscles D and E are slack and motionless; the more so because the animal spirits which they contain flow freely from one muscle to the other, from e by f to d and conversely from d by g to e. When the spirits tend to enter the tubes, bf, cg, however, with an equal force from both sides, they immediately close the two passages g and f and fill out the muscles D and E as much as possible, thus causing them to hold the eye firmly in whatever position they find it.

Again, if the animal spirits from the brain tend to flow with more force through bf than cg, they close the valve g and open f—either more or less, in proportion to their strength—through which the spirits in muscle E pass to muscle D by the tube ef, at a speed in proportion to the size of the opening at f, so that muscle D shortens, because the spirits cannot flow out of it, while E lengthens, and thus the eye is turned towards D. On the other hand if the spirits flow with greater force through cg than through bf they close valvule f and open g, so that the spirits from muscle D go back at once by the tube dg to muscle E, which thus becomes shortened and pulls the eye towards that side.

These spirits are like a wind or a very subtle flame and they are bound to flow very rapidly from one muscle to another whenever they can find a passage; and this though no force guides them, but only their inclination to move about according to the laws of nature. And though they are very subtle and lively, yet when they flow into a muscle they cause it to become stiff and swollen, just as air in a balloon makes it hard and stretches the substance in which it is contained.

ROBERT WHYTT

Robert Whytt (1714-1766), a neurologist of Edinburgh, approached the physiology of the central nervous system in the modern spirit, extirpating known regions of the central nervous system and studying how animals reacted thereafter to various stimuli. His book,[3] in which the results are described, is one of the most remarkable in the history of neurology. In it he establishes that the spinal cord is essential for reflex action and describes the pupillary response to light—which is still known as "Whytt's reflex"—observing that destruction of the anterior *corpora quadrigemina* abolished the reaction. The following passage indicates that he also grasped fully the mechanism and significance of reflex action.

---

[3] Whytt, R. *An essay on the vital and other involuntary motions of animals.* Edinburgh: Hamilton, Balfour and Neill, x+392 pp., 1751 (pp. 288-291). For an excellent account of Whytt see Leonard Carmichael's "Robert Whytt: a contribution to the history of physiological psychology." *Psych. Review,* vol. 34, pp. 287-304, 1927.

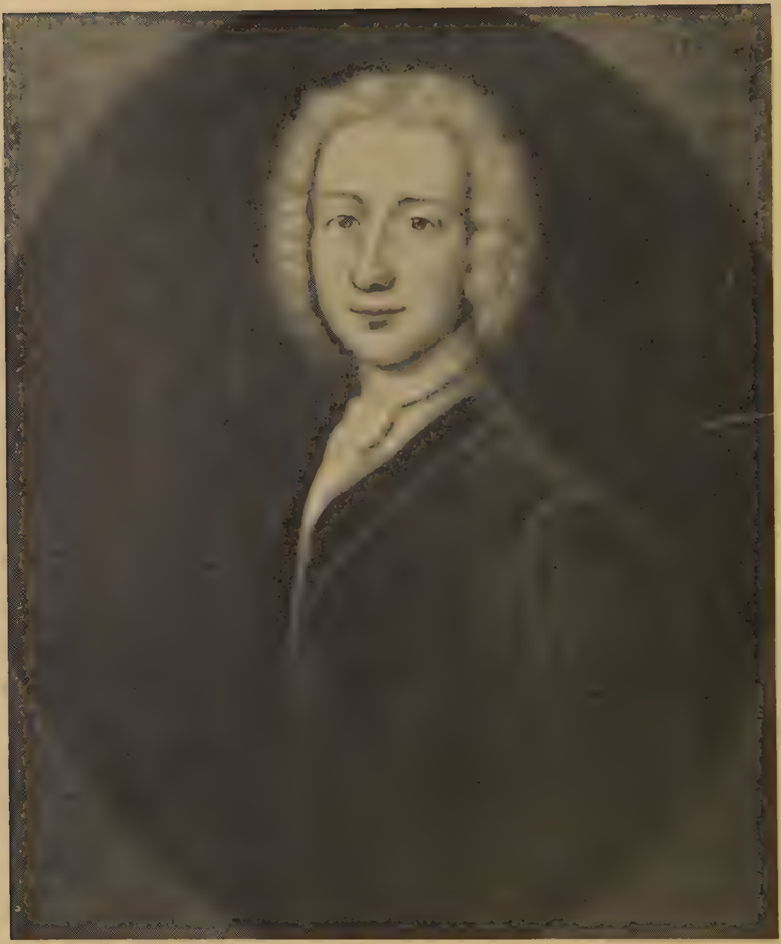


FIGURE 54. The portrait of Whytt which hangs in the Royal College of Physicians, Edinburgh.

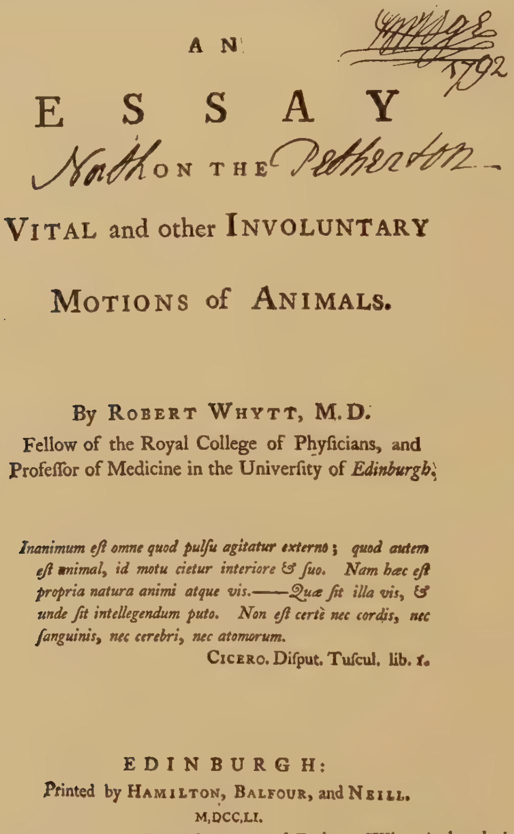
To the element within the central nervous system which received sensory impressions he applied the term 'sentient principle' and inferred that, unlike the 'rational soul' of Descartes, it was diffused throughout the brain and spinal cord.

'VITAL' MOTIONS

FURTHER, the motions excited by any pain, or irritation, are so instantaneous, that there can be no time for the exercise of reason, or a comparison of ideas in order to their performance; but they seem to follow as a necessary and immediate consequence of the disagreeable perception. And as the DEITY seems to have implanted in our minds a kind of SENSE respecting *Morals,* whence we approve of some actions, and disapprove of others, almost instantly, and without any previous reasoning about their fitness or unfitness; a FACULTY of singular use, if not absolutely necessary for securing the interests of virtue among such creatures as men! so, methinks, the analogy will appear very easy and natural, if we suppose our minds so formed and connected with our bodies, as that, in consequence of a *stimulus* affecting any organ, or of an uneasy perception in it, they shall immediately excite such motions in this or that organ, or part of the body, as may be most proper to remove the irritating cause; and this, without any previous rational conviction of such motions being necessary or conductive to this end. Hence, men do not eat, drink, or propagate their kind, from deliberate views of preserving themselves or their species, but merely in consequence of the uneasy sensations of hunger, thirst, *&c.*

THE mind, therefore, in producing the vital and other involuntary motions, does not act as a rational, but as a sentient principle; which, without reasoning upon this matter, is as necessarily determined by an ungrateful sensation or *stimulus* affecting the organs, to exert its power, in bringing about these motions, as is a balance, while, from mechanical laws, it preponderates to that side where the greatest weight prevails.

THE general and wise intention of all the involuntary motions, is the removal of every thing that irritates, disturbs, or hurts the body: hence, those violent motions of the heart, in the beginning of fevers, small-pox, measles, *&c.* when frequently the blood, from its being affected by the mixture of some peculiar *miasma,* acts as a stronger *stimulus* than usual upon this organ. Nevertheless, as, in many instances, the very best things may, by excess, become hurtful; so this endeavour to free the body, or any of its parts, from what is noxious, is unhappily, sometimes, so strong and vehement, as to threaten the entire destruction of the animal fabric. But, in the main, this FACULTY must be confessed highly useful and beneficial; since, without it, we should constantly have cherished in our bodies the lurking principles of diseases, slowly indeed and by imperceptible degrees, but not less surely, ruining our health and constitutions.



AN 1792

ESSAY

Nath ON THE Petherton

VITAL and other INVOLUNTARY

MOTIONS of ANIMALS.

By ROBERT WHYTT, M.D.
Fellow of the Royal College of Phyſicians, and
Profeſſor of Medicine in the Univerſity of *Edinburgh*.

Inanimum eſt omne quod pulſu agitatur externo; quod autem eſt animal, id motu cietur interiore & ſuo. Nam hæc eſt propria natura animi atque vis.——Quæ ſit illa vis, & unde ſit intellegendum puto. Non eſt certè nec cordis, nec ſanguinis, nec cerebri, nec atomorum.
CICERO. Diſput. Tuſcul. lib. 1.

EDINBURGH:
Printed by HAMILTON, BALFOUR, and NEILL.
M,DCC,LI.

FIGURE 55. The title-page of Robert Whytt's book in which the theory of reflex action was set forth, 1751.

UPON the whole, there seems to be in man one sentient and intelligent PRINCIPLE, which is equally the source of life, sense and motion, as of reason; and which, from the law of its union with the body, exerts more or less of its power and influence, as the different circumstances of the several organs actuated by it may require. That this principle operates upon the body, by the intervention of something in the brain or nerves, is, I think, likewise probable; though, as to its particular nature, I presume not to allow myself in any uncertain conjectures; but, perhaps, by means of this connecting *medium,* the various impressions, made on the several parts of the body either by external or internal causes, are transmitted to, and perceived by the mind; in consequence of which it may determine the nervous influence variously into different organs, and so become the cause of all the vital and involuntary motions, as well as of the animal and voluntary. It seems to act necessarily, and as a sentient principle only, when its power is exerted in causing the former; but, in producing the latter, it acts freely, and both as a sentient and rational agent.

GEORGIUS PROCHASKA

Georgius Prochaska (1749-1820), a brilliant anatomist of Vienna, known throughout the continent of Europe on account of his attractive lectures and writings, attempted more precise allocation of the elements of a reflex to known structures in the nervous system. He occupies an important position in the history of psychology for his introduction of the conception of a "sensorium commune"—that region of the central nervous system which "reflects" to the motor nerves the sensory impressions received by the brain. There is no suggestion in the writings of Prochaska of sensory and motor roots, but sensory and motor fibres are tacitly assumed. The following excellent translation[4] appeared in 1839 in an anonymous work, presumably by Alexander Walker, entitled *Documents and dates of modern discoveries in the nervous system.*

INVOLUNTARY MOTIONS REFLECTED FROM THE SENSORIUM COMMUNE

What are the sensorium commune, its functions, and its seat?

External impressions, which are made upon the sensorial nerves, are propagated rapidly through their whole length to their origin; where, when they have arrived, they are reflected according to a certain law, and pass into certain and corresponding motor nerves, through which, again rapidly propagated even to the muscles, they excite certain and determinate motions. This place, in which, as in a centre, the nerves appropriated to sense as well as motion, meet and communicate, and in which the impressions of the sensorial nerves are reflected upon the motor nerves, is called the sensorium commune—a term already received by most physiologists.

---

[4] Prochaska's theory of a "sensorium commune" appeared in his *Adnotationum academicarum fasciculi tres,* fasciculus III, which bears the title "De functionibus systematis nervosi et observationes anatomico-pathologicæ." The "Adnotationum" was published at Prague, the first fasciculus in 1780 and the last in 1784. The passage translated above was reprinted in Latin at Vienna in 1800 in Prochaska's *Opera minorum anatomici-physiologici et pathologici argumenti,* and occurs in the second volume on page 150 *et seq.*

The whole cerebrum and cerebellum certainly do not seem to belong to the composition of the sensorium commune: these parts of the nervous system appear to be rather the instruments which the mind uses immediately in the performance of the actions termed animal; but it seems not improbable that the sensorium commune, properly so called, extends to the medulla oblongata, the crura cerebri and cerebelli, even to part of the thalami optici, and to the whole spinal marrow, in a word, as widely as the origin of the nerves. That the sensorium commune extends to the spinal marrow, we learn from the motions remaining in decapitated animals, which could not take place without the consent and cooperation of the nerves arising from the spinal marrow; for if a decapitated frog be pricked, not only does it retract the punctured part, but it crawls and leaps, which could not be without the consent of the sensorial and motor nerves, of which consent the seat must be in the spinal marrow, the part of the sensorium commune remaining.

The reflection of sensorial into motory impressions, which takes place in the sensorium commune, does not obey mere physical laws, where the angle of reflection is equal to the angle of incidence, and where action and reaction are equal, but it follows peculiar laws written, as it were, by nature, in the medullary pulp of the sensorium, which we can know only by their effects, and not discover by our imagination. Nevertheless, a general law, according to which the sensorium commune reflects sensorial into motor impressions, is our preservation: so that certain motory impressions follow external impressions hurtful to the body, producing motions tending to ward off and remove the source of injury; and, on the contrary, internal or motor impressions follow external or sensorial impressions beneficial to us, producing motions calculated to perpetuate that benefit. Many examples certainly prove this general law of the reflections of the sensorium commune, of which it will be sufficient to adduce a few. Irritation of the internal membrane of the nostrils excites sneezing, because that impression, made by irritation of the olfactory nerves, is by them carried to the sensorium commune, is there reflected, according to a certain law, upon motor nerves going to the muscles appropriated to respiration, and, through these, produces a forcible expiration through the nose, in which, by the air forcibly passing, the irritation is removed. So it happens when any irritation is caused to the wind-pipe by a crumb of bread or a drop of liquid falling into it: this irritation, carried to the sensorium commune, and thence reflected upon the nerves appropriated to respiratory motion, excites a forcible cough, the most apt remedy for expelling the irritant, which does not cease until that irritant is removed. If a friend approaches our eye with his finger, although we are persuaded that no harm will be done to us, yet that impression carried by the optic nerve to the sensorium commune, is in the sensorium so reflected upon the nerves appropriated to the motion of the eyelids, that the palpebrae are involuntarily closed so as to avoid the contact of the finger. These and innumerable other examples that might be adduced, show manifestly how much the reflection of sensorial into motor impressions by the sensorium commune regards the preservation of our body. On this account, Tissot properly enumerates the action of the sensorium commune amongst those powers of which the end and union constitute the nature of our living body.

As, therefore, the principal function of the sensorium commune consists in the reflection of sensorial into motor impressions, it is to be observed, that this reflection takes place whether the mind be conscious or unconscious of it. The motion of the heart, of the stomach, and of the intestines, certainly in no respect depend on the consciousness of the mind; but as no muscular motion can be excited, unless a stimulus applied to the sensorial nerves passes by a certain reflection to the motor nerves, and excites muscular contraction, so it is certain that the reflection of impressions proper for inducing these motions, if they take place in the sensorium commune, takes place without the consciousness of the mind. But it is asked whether these impressions ascend to the sensorium commune, to be reflected, or whether, without making this circuit, they are more quickly reflected by the ganglia, whence these parts have many nerves. More on this point hereafter. But that the reflections of sensorial into motor impressions take place quite unconsciously in the sensorium commune, we learn from certain actions remaining in apoplectic patients, in whom all consciousness is destroyed; for they have a strong pulse, breathe strongly, and often even raise the hand unconsciously to the part affected. The sensorium commune acts also without consciousness in producing the convulsive motions of epileptic patients, and even those retractions of the limbs when slightly pricked or pinched, which are sometimes observed in profound sleep, besides motion of the heart and respiration. To these we must add all those motions which for some time remain in the body of a decapitated man, or other animal, and are excited by pinching the body, but especially the spinal marrow, which certainly occur without consciousness, and are governed by the residual part of the sensorium commune, which is in the spinal marrow. All these actions arise from the organisation and physical laws proper to the sensorium commune, and are, therefore, spontaneous and automatic. Those actions, which take place in the animal body with consciousness, are either such, that the mind has no power over its will, or such as the mind can coerce or impede at will: the former, as they are ruled by the sensorium commune alone, in as far as it does not depend upon the mind, are also automatic actions, not less than those which are performed unconsciously; such are sneezing from a stimulus applied to the nostrils, cough from a stimulus applied to the trachea, vomiting from irritation of the fauces, or from an emetic, tremor and convulsions in chorea S. Viti, and in the paroxysms of intermittent fever, &c. But the actions which the mind directs and moderates by its power, although the sensorium commune has its part in producing them, we call, nevertheless, animal, not automatic.

ALEXANDER WALKER

Alexander Walker (1779-1852), an eccentric of the Edinburgh School of Anatomy, deserves credit for having insisted, prior to Bell and Magendie, upon the separate functions of the posterior and anterior roots of spinal nerves. Unfortunately he appears to have based his inferences purely upon anatomy and he assigned to the anterior roots the function of sensibility and to the posterior roots motor power. He was deeply perturbed that no one of his time gave him credit for his speculations, and he died still believing that the posterior roots were motor and the anterior sensory. The following passage[5] from his paper published in 1809 is included here as one of the curiosities of physiological literature. Walker was a scholarly man whose translations from French, German and Latin are above reproach (see his anonymous *Documents and dates of modern discoveries in the nervous system,* London, 1839). Struthers[6] notes that he was forced to leave London for having pointed out to a group of fellow students that the great Abernethy, during an operation which they witnessed, had tied off a nerve-trunk when intending to ligate the subclavian artery.

Thus, then, it is proved to us, that medullary action commences in the organs of sense; passes, in a general manner, to the spinal marrow, by the anterior fasciculi of the spinal nerves, which are, therefore, nerves

[5] Walker, A. "New anatomy and physiology of the brain in particular, and of the nervous system in general." *Archives of Universal Science,* vol. 3, p. 172 *et seq.,* 1809.

[6] Struthers, J. *Historical sketch of the Edinburgh anatomical school.* Edinburgh: Maclachlan and Stewart, 94 pp., 1867 (p. 77).

of sensation, and the connexions of which with the spinal marrow or brain must be termed their spinal or cerebral terminations; ascends through the anterior columns of the spinal marrow which are, therefore, its ascending columns; passes forward through the inferior fasciculi of the medulla oblongata, and then through the crura cerebri; extends forward, outward and upward through the corpora striata; and reaches the hemispheres of the cerebrum itself. This precisely is the course of its ascent to the sensorium commune.

From the posterior part of the medulla of the hemispheres, it returns by the thalami, passing backward, inward and downward; flows backward in the fasciculi under the nates and testes; backward and upward through the processus cerebelli and testes or anterior peduncles of the cerebellum; and thus reaches the medulla of the cerebellum itself.

From the cerebellum, it descends through the posterior columns of the spinal marrow, which are, therefore, its descending columns; and expands through the posterior fasciculi of all the nerves, which are, therefore, the nerves of volition, and the connexions of which with the spinal marrow or brain must be termed their spinal or cerebellic origins. This precisely is the course of its descent from the sensorium commune toward the muscular system.

Now, from this course, it is evident, that impressions acting on the organs of sense, and there producing sensations, will reach, by this route, the sensorium commune, and there constitute perception, or, in other words, will have their influence diffused from this central point, and rendered universally cognizable to the system; for all the actions which take place in this system must be cognizable to it, and even the action of other systems can only be cognizable by means of this one.

Volition would similarly appear to consist in the transmission of the impulse from the cerebellum, the new modification which, from its structure, that impulse must undergo, and its rapid descent through the posterior columns to the muscular organs.

CHARLES BELL

Sir Charles Bell (1774-1842), an anatomist born in Edinburgh, was a prolific writer whose beautifully illustrated anatomical works still remain one of the chief desiderata of anatomical collectors. His claims to priority in the discovery of the functions of the anterior and posterior roots of the spinal cord have been the subject of prolonged controversy. Those who wish authoritative information should consult Norman Moore's life of Bell in the *Dictionary of Na-*

tional Biography, A. D. Waller's and Keith's correspondence in the *Lancet,* 1911-12, and Carmichael's recent excellent account of Bell.[9] Bell put forward his beliefs in 1811 in a privately printed pamphlet entitled *A new idea of the anatomy of the brain submitted for the observation of his friends.* As only two copies of the tract are known to exist, it seems desirable to give in full all that relates to the discovery. It will be evident to anyone who studies the tract that Bell's real claim rests on having demonstrated convincingly the motor functions of the anterior roots. In this tract he certainly did not prove the sensory functions of the posterior roots. In an article published in the *Philosophical Transactions* in 1821 the conception was published, but in reserved and halting terms.[10] This paper was reprinted several times after Magendie's discovery had been announced and Bell was clearly guilty of making changes in the original text, giving more definite shape to the theory, yet retaining the date 1821. Though one hesitates to pass judgment upon claims to priority, one cannot doubt that Bell was dishonest and that the chief credit of elucidating the function of the posterior as well as the anterior roots belongs to Magendie. It will be observed that he had clearly in mind the principle of specific nerve energies.

IDEA OF A NEW ANATOMY OF THE BRAIN; SUBMITTED FOR THE OBSERVATION OF HIS FRIENDS;

Note.

The want of any consistent history of the brain and nerves, and the dull unmeaning manner which is in use of demonstrating the brain, may authorize any novelty in the manner of treating the subject.

I have found some of my friends so mistaken in their conceptions of the object of the demonstrations which I have delivered in my lectures, that I wish to vindicate myself at all hazards. They would have it that I am in search of the seat of the soul; but I wish only to investigate the structure of the brain, as we examine the structure of the eye and ear.

It is not more presumptuous to follow the tracts of nervous matter in the brain, and to attempt to discover the course of sensation, than it is to trace the rays of light through the humours of the eye, and to say, that the retina is the seat of vision. Why are we to close the investigation with the discovery of the external organ.

It would have been easy to have given this essay an imposing splendour, by illustrations and engravings of the parts, but I submit it as a sketch to those who are well able to judge of it in this shape.

---

[9] Carmichael, L. "Sir Charles Bell: a contribution to the history of physiological psychology." *Psych. Review,* vol. 33, pp. 188-217, 1926.

[10] Bell, C. "On the nerves; giving an account of some experiments on their structure and functions, which lead to a new arrangement of the system." *Phil. Trans.,* vols. 110 and 111, 1821.

The prevailing doctrine of the anatomical schools is, that the whole brain is a common sensorium; that the extremities of the nerves are organized, so that each is fitted to receive a peculiar impression; or that they are distinguished from each other only by delicacy of structure, and by a corresponding delicacy of sensation; that the nerve of the eye, for example, differs from the nerves of touch only in the degree of its sensibility. It is imagined that impressions, thus differing in kind, are carried along the nerves to the sensorium, and presented to the mind; and that the mind, by the same nerves which receive sensation, sends out the mandate of the will to the moving parts of the body.

It is further imagined, that there is a set of nerves, called vital nerves, which are less strictly connected with the sensorium, or which have upon them knots, cutting off the course of sensation, and thereby excluding the vital motions from the government of the will.

This appears sufficiently simple and consistent, until we begin to examine anatomically the structure of the brain, and the course of the nerves—then all is confusion: the divisions and subdivisions of the brain, the circuitous course of nerves, their intricate connections, their separation and re-union, are puzzling in the last degree, and are indeed considered as things inscrutable. Thus it is that he who knows the parts the best, is most in a maze, and he who knows least of anatomy, sees least inconsistency in the commonly received opinion.

In opposition to these opinions, I have to offer reasons for believing that the cerebrum and cerebellum are different in function as in form; that the parts of the cerebrum have different functions; and that the nerves which we trace in the body are not single nerves possessing various powers, but bundles of different nerves, whose filaments are united for the convenience of distribution, but which are distinct in office, as they are in origin from the brain.

That the external organs of the senses have the matter of the nerves adapted to receive certain impressions, while the corrsponding organs of the brain are put in activity by the external excitement: that the idea or perception is according to the part of the brain to which the nerve is attached, and that each organ has a certain limited number of changes to be wrought upon it by the external impression.

That the nerves of sense, the nerves of motion, and the vital nerves, are distinct through their whole course, though they seem sometimes united in one bundle; and that they depend for their attributes on the organs of the brain to which they are severally attached.

The view which I have to present will serve to show why there are divisions, and many distinct parts in the brain; why some nerves are simple in their origin and distribution, and others intricate beyond description. It will explain the apparently accidental connection between the twigs of nerves. It will do away with the difficulty of conceiving how sensation and volition should be the operation of the same nerve at the same moment. It will shew how a nerve may lose one property and retain another; and it will give an interest to the labours of the anatomist in tracing the nerves.

It is admitted that neither bodies nor the images of bodies enter the brain. It is indeed impossible to believe that colour can be conveyed along a nerve; or the vibration in which we suppose sound to consist can be retained in the brain: but we can conceive, and have reason to believe, that an impression is made upon the organs of the outward senses, when we see, or hear, or taste.

In this enquiry, it is most essential to observe, *that while each organ of sense is provided with a capacity of receiving certain changes to be played upon it, as it were, yet each is utterly incapable of receiving the impression destined for another organ of sensation.* [Editor's italics]

It is also very remarkable that an impression made on two different nerves of sense, though with the same instrument, will produce two distinct sensations; and the ideas resulting will only have relation to the organ affected.

As the announcing of these facts forms a natural introduction to the anatomy of the brain, which I am about to deliver, I shall state them more fully.

There are four kinds of papillae on the tongue, but with two of those only we have to do at present. Of these, the papillae of one kind form the seat of the sense of taste; the other papillae (more numerous and smaller) resemble the extremities of the nerves in the common skin, and are the organs of touch in the tongue. When I take a sharp steel point and touch one of these papillae, I feel the sharpness. The sense of touch informs me of the shape of the instrument. When I touch a papilla of taste, I have sensation similar to the former. I know not that a point touches the tongue, but I am sensible of a metallic taste, and the sensation passes backward on the tongue.

In the operation of couching the cataract, the pain of piercing the retina with a needle is not so great as that which proceeds from a grain of sand under the eyelid. And although the derangement of the stomach sometimes marks the injury of an organ so delicate, yet the pain is occasioned by piercing the outward coat, not by the affection of the expanded nerve of vision.

If the sensation of light were conveyed to us by the retina, the organ of vision, in consequence of that organ being as much more sensible than the surface of the body as the impression of light is more delicate than that pressure which gives us the sense of touch; what would be the feelings of a man subjected to an operation in which a needle were pushed through the nerve? Life could not bear so great a pain.

But there is an occurrence during this operation on the eye, which will direct us to the truth: when the needle pierces the eye, the patient has the sensation of a spark of fire before the eye.

This fact is corroborated by experiments made on the eye. When the eyeball is pressed on the side, we perceive various coloured light. Indeed, the mere effect of a blow on the head might inform us, that sensation depends on the exercise of the organ affected, not on the impression conveyed to the external organ; for by the vibration caused by the blow, the ears ring, and the eye flashes light, while there is neither light nor sound present.

It may be said that there is here no proof of the sensation being in the brain more than in the external organ of sense. But when the nerve of a stump is touched, the pain is as if in the amputated extremity. If it be still said that this is no proper example of a peculiar sense existing without its external organ, I offer the following example: Quando penis glandem exedat ulcus, et nihil nisi granulatio maneat, ad extremam tamen nervi pudicae pactem ubi terminatur sensus supersunt, et exquisitissima sensus gratificatio.

I found that injury done to the anterior portion of the spinal marrow, convulsed the animal more certainly than injury done to the posterior portion; but I found it difficult to make the experiment without injuring both portions.

Next, considering that the spinal nerves have a double root, and being of opinion that the properties of the nerves are derived from their connections with the parts of the brain, I thought that I had an opportunity of putting my opinion to the test of experiment, and of proving at the same time that nerves of different endowments were in the same cord, and held together by the same sheath.

On laying bare the roots of the spinal nerves, I found that I could cut across the posterior fasciculus of nerves, which took its origin from *the posterior portion of the spinal marrow without convulsing the muscles of the back; but that on touching the anterior fasciculus with the point of a knife, the muscles of the back were immediately convulsed.* Such were my reasons for concluding that the cerebrum and the cerebellum were parts distinct in function, and that every nerve possessing a double function obtained that by having a double root. I now saw the meaning of the double connection of the nerves with the spinal marrow; and also the cause of that seeming intricacy in the connections of nerves throughout their course, which were not double at their origins.

The spinal nerves being double, and having their roots in the spinal marrow, of which a portion comes from the cerebrum and a portion from the cerebellum, they convey the attributes of both grand divisions of the brain to every part; and therefore the distribution of such nerves is simple, one nerve supplying its distinct part. But the nerves which come directly from the brain, come from parts of the brain which vary in operation; and in order to bestow different qualities on the parts to which the nerves are distributed, two or more nerves must be united in their course or at their final destination. Hence it is that the first nerve must have branches of the fifth united with it: hence the *portio dura* of the seventh pervades every where the bones of the cranium to unite with the extended branches of the fifth: hence the union of the third and fifth in the orbit: hence the ninth and fifth are both sent to the tongue: hence it is, in short, that no part is sufficiently supplied by one single nerve, unless that nerve be a nerve of the spinal marrow, and have a double root, a connection (however remotely) with both the cerebrum and cerebellum. Such nerves as are single in their origin from the spinal marrow will be found either to unite in their course with some other nerve, or to be such as are acknowledged to be peculiar in their operation.

The eighth nerve is from the portion of the medulla oblongata which belongs to the cerebellum: the ninth nerve comes from the portion which belongs to the cerebrum. The first is a nerve of the class called vital nerves, controlling secretly the operations of the body; the last is the motor nerve of the tongue, and is an instrument of volition. Now the connections formed by the eighth nerve in its course to the viscera are endless; it seems nowhere sufficient for the entire purpose of a nerve; for every where it is accompanied by others, and the ninth passes to the tongue, which is already profusely supplied by the fifth.

If this be not at once obvious, it proceeds only from the circumstance that the nerves take their origin from the different parts of the brain; and while those nerves are considered as simple cords, this circumstance stands opposed to the conclusion which otherwise would be drawn. A nerve having several roots implies that it propagates its sensation to the brain generally. But when we find that the several roots are distinct in their endowment, and are, in respect to office, distinct nerves; then the conclusion is unavoidable, that the portions of the brain are distinct organs of different functions.

To arrive at any understanding of the internal parts of the cerebrum, we must keep in view the relation of the nerves, and must class and distinguish the nerves, and follow them into its substance. If all ideas originate in the mind from external impulse, how can we better investigate the structure of the brain than by following the nerves, which are means of communication betwixt the brain and the outward organs of the senses?

The nerves of sense, the olfactory, the optic, the auditory, and the gustatory nerves, are traced backwards into certain tubercles or convex bodies in the base of the brain. And I may say, the nerves of sense either form tubercles before entering the brain, or they enter into those convexities in the base of the cerebrum. These convexities are the constituent parts of the cerebrum, and are in all animals necessary parts of the organs of sense; for as certainly as we discover an animal to have an external organ of sense, we find also a medullary tubercle; whilst the superiority of animals in intelligence is shown by the greater magnitude of the hemispheres or upper part of the cerebrum.

The convex bodies which are seated in the lower part of the cerebrum, and into which the nerves of sense enter, have extensive connection with the hemispheres on their upper part. From the medullary matter of the hemispheres, again, there pass down, converging to the crura, striae, which is the medullary matter taking upon it the character of a nerve; for from the crura cerebri, or its prolongation in the anterior fasciculi of the spinal marrow, go off the nerves of motion.

But with these nerves of motion which are passing outward there are nerves going inwards; nerves from the surfaces of the body; nerves of touch; and nerves of peculiar sensibility, having their seat in the body or viscera. It is not improbable that the tracts of cineritious matter which we observe in the course of the medullary matter of the brain, are the seat of such peculiar sensibilities; the organs of certain powers which seem resident in the body.

Again if those parts of the brain which are directly connected with the nerves, and which resemble them in structure, give pain when injured, and occasion convulsion to the animal as the nerves do when they are injured; and if, on the contrary, such parts as are more remote from the nerves, and of a different structure, produce no such effect when injured, we may conclude, that the office of the latter parts is more allied to the intellectual operations, less to mere sensation.

I have found at different times all the internal parts of the brain diseased without loss of sense; but I have never seen disease general on the surfaces of the hemispheres without derangement or oppression of the mind during the patient's life. In the case of derangement of mind, falling into lethargy or stupidity, I have constantly found the surface of the hemispheres dry and preternaturally firm, the membrane separating from it with unusual facility.

If I be correct in this view of the subject, then the experiments which have been made upon the brain tend to confirm the conclusions which I should be inclined to draw from strict anatomy; viz. that the cineritious and superficial parts of the brain are the seat of the intellectual functions. For it is found that the surface of the brain is totally insensible, but that the deep and medullary part being wounded, the animal is convulsed and pained.

FRANÇOIS MAGENDIE

François Magendie (1783-1855), the pioneer experimental physiologist of France, introduced a new era in physiology. Impetuous, hard-working, versatile, Magendie left his mark in almost every branch of physiological thought, and though he paved the way for the great developments in experimental physiology of the 19th century, his contribution was really more one of isolated facts rather than of broad generalizations. He was fearless, and at times unnecessarily cruel, but he invariably triumphed over the avalanche of criticism which frequently overtook him. In 1821 he began to publish the first journal in French to be devoted exclusively to physiology; it bore the title *Journal de Physiologie expérimentale et pathologique* and passed through ten volumes (1821-1831). His first two papers on the functions of the roots of spinal nerves,[7] translated in full below, appeared in the second volume of this journal. The translations given are those of Alexander Walker[8] which are lucid and accurate, and have the advantage of being contemporary.

[7] Magendie, F. "Expériences sur les fonctions des racines des nerfs rachidiens." *Jour. Physiol. expér. et path.*, tom. 2, pp. 276-279, 1822. "Expériences sur les fonctions des racines des nerfs qui naissent de la moëlle épinière." *Ibid.*, tom. 2, pp. 366-371, 1822.

[8] Walker, A. *Documents and dates of modern discoveries in the nervous system.* London: John Churchill, xii+172 pp., 1839 (pp. 87-101).

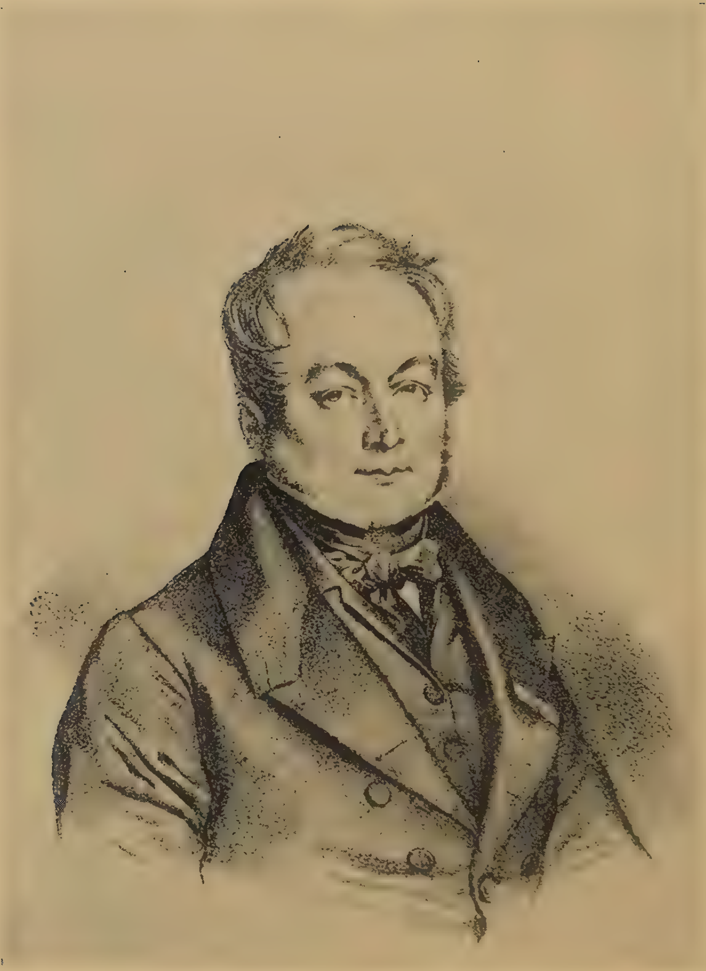


FIGURE 56. François Magendie (1783-1855).

EXPERIMENTS UPON THE FUNCTIONS OF THE ROOTS OF THE SPINAL NERVES

I had long been desirous of making the experiment of dividing in an animal the posterior roots of the nerves which arise from the spinal marrow. I had several times made the attempt, without being able to succeed, on account of the difficulty of opening the vertebral canal without injuring the spinal marrow, and consequently without destroying or at least seriously wounding the animal. Last month there was brought to my laboratory a litter of eight puppies, six weeks old; these animals appeared to me very suitable for a new attempt at opening the vertebral canal. I was able indeed, with the help of a very sharp scalpel, and I may say at a single cut, to expose the posterior half of the spinal marrow surrounded by its envelopes. There only remained for the complete exposure of this organ to cut the dura-mater which surrounds it: this I did with facility; I then had a complete view of the posterior roots of the lumbar and sacral pairs, and in lifting them up successively with the points of a small pair of scissors, I was able to cut them on one side, the spinal marrow remaining untouched. I was ignorant what might be the result of this attempt; I reunited the wound by a suture, and then observed the animal; I at first thought the member corresponding to the cut nerves, was entirely paralysed; it was insensible to the strongest prickings and pressures, it seemed to me also incapable of moving; but soon, to my great surprise, I saw it move in a manner very apparent, although sensibility was entirely extinct. A second and third experiment gave me exactly the same result; I began to think it probable that the posterior roots of the spinal nerves might have different functions from the anterior roots, and that they were more particularly destined for sensation.

It naturally occurred to the mind to cut the anterior roots, leaving the posterior untouched; but such an enterprise was more easily conceived than executed; how expose the anterior part of the spinal marrow, without interfering with the posterior roots? I confess that the thing at first appeared to me to be impossible; nevertheless for two days I continued to think of it, and at last I decided to endeavour to pass before the posterior roots, a sort of cataract knife, the blade of which, being very narrow, would permit of my cutting the roots, by pressing them with the sharp side of the instrument, against the posterior surface of the body of the vertebræ; but I was obliged to renounce this method on account of the large veins which the canal contains on that side, and which I opened at each progressive movement. In making these attempts, I perceived that by pulling the vertebral dura-mater, the anterior roots might be seen united in bundles, exactly where they pierce that membrane. I wanted nothing more, and in a few moments I had cut all the pairs which I wished to divide. As in the preceding experiments, I made the section on one side only, in order to have a point of comparison. It may be conceived with what curiosity I observed the effects of this section: they were not doubtful, the member was completely immovable and flaccid, at the same time preserving an unequivocal sensibility. Finally, that nothing might be neglected, I cut the anterior and posterior roots at the same time; there ensued absolute loss both of sensibility and of motion.

I have repeated and varied these expirements upon several species of animals: the results just announced were confirmed in the most complete manner, both for the posterior and anterior members. I am pursuing these researches, and I shall give a more detailed recital of them in the following number; it is sufficient for me at present to be able to advance as positive, that the anterior and posterior roots of the nerves which arise from the spinal marrow, have different functions, that the posterior appear more particularly destined to sensibility, whilst the anterior seem more especially allied to motion.

EXPERIMENTS UPON THE FUNCTIONS OF THE ROOTS OF THE NERVES WHICH ARISE FROM THE SPINAL MARROW.

The facts which I announced in the preceding number are too important to be passed over without my seeking to throw light upon them by new researches.

I at first wished to ascertain if it might not be possible to cut the anterior and posterior roots of the spinal nerves without opening the great canal of the vertebral dura-mater; because, by exposing the spinal marrow to the air and to a cold temperature, the nervous action is sensibly weakened, and consequently the results sought for are obtained in a manner but little apparent.

The anatomical position of the parts did not render the thing impossible; for each bundle of spinal roots goes for some time in a particular canal before uniting and confounding itself with the other bundle. I found indeed that with the help of scissors blunt at the points, a sufficient quantity of the plates and lateral parts of the vertebræ may be taken away to expose the ganglion of each lumbar pair;

and then with a small stylet there is not much difficulty in separating the canal which contains the posterior roots, and the section becomes easy. This mode of making the experiment gave me the same results as those I had previously observed; but as the experiment is much longer and more laborious than the preceding one in which the great canal of the spinal dura-mater is opened, I do not think that this mode of making the experiment should be followed in preference to the first.

I afterwards wished to submit to more particular proof the results of which I have previously spoken. Every one knows that nux vomica determines both in man and animals, general and very violent tetanic convulsions. I was curious to ascertain if these convulsions would still take place in a member in which the nerves of motion had been cut, and if they would appear to be as strong as usual, a section of the nerves of sensation having been made. The result accorded entirely with the preceding; that is to say in an animal in which the posterior roots were cut, the tetanus was complete and as intense as if the spinal nerves had been untouched: on the contrary, in an animal in which I had cut the nerves of motion of one of the posterior members, the members remained supple and immovable at the time when, under the influence of the poison, all the other muscles of the body suffered the most violent tetanic convulsions.

On directly irritating the nerves of sensation, or the posterior spinal roots, would contractions be produced? Would a direct irritation of the nerves of motion excite pain? These were the questions which I asked myself and which experience alone could resolve.

With this view, I began to examine the posterior roots or the nerves of sensation. The following are the results of my observations: in pinching, pulling, pricking these roots, the animal gives signs of pain; but it is not to be compared in intensity with that which occurs if the spinal marrow be only slightly touched at the part where these roots arise. Nearly every time that these posterior roots are thus excited, contractions are produced in the muscles to which the nerves are distributed; these contractions are however but slightly marked, and infinitely weaker than if the spinal marrow itself be touched. If one of the posterior bundles of roots be cut at once, a general movement is produced in the member to which the bundle goes.

I have repeated the same experiments upon the anterior bundles, and I have obtained analogous results, but in an inverse sense; for the contractions excited by the pinching, pricking, &c. are extremely strong and even convulsive, whilst the signs of sensibility are scarcely visible. These facts then are confirmative of those already announced; only they seem to establish that sensation does not belong exclusively to the posterior roots, any more than motion to the anterior.

Nevertheless a difficulty might arise. When, in the preceding experiments, the roots were cut, they were continuous with the spinal marrow: might not the disturbance communicated to the latter have been the real origin, either of the contractions or of the pain felt by the animals? To remove this doubt, I repeated the experiments, after having separated the roots from the spinal marrow; and I ought to say that, with the exception of two animals in which I saw contractions upon pinching and pulling the anterior and posterior bundles, in all the rest I did not observe any sensible effect from the irritation of the anterior or posterior roots thus separated from the spinal marrow.

I had still to make another kind of experiment on the spinal roots; that of galvanism. By its means, I accordingly excited these parts, first leaving them in their ordinary state, and afterwards cutting them at their spinal extremities to place them upon an isolating body. In these various cases, I obtained contractions from each sort of roots; but those which followed the excitation of the anterior roots were in general much stronger and more complete than those which took place when the electric current operated upon the posterior. The same phenomena took place either by applying the zinc or copper pole to the nerve.

It now remains for me to give an account of my researches to endeavour to follow motion and sensation distinctly beyond the roots of the nerves, that is to say, into the spinal marrow; this is the subject of my present occupation.

Before finishing this article, I ought to give some further explanation as to the novelty of the results which I have announced.

When I wrote the note contained in the preceding number, I believed I was the first who had thought of dividing the roots of the spinal nerves; but I was soon undeceived by a small work by Mr. Shaw, which this young and laborious practitioner had the politeness to send me as soon as he had received the number of my journal. It is said in that work that Mr. Charles Bell made this section thirteen years ago, and that he had discovered that the section of the posterior roots did not prevent the continuance of motion. Mr. Shaw adds that Mr. Charles Bell had stated this result in a small pamphlet printed solely for the use of his friends, but not for publication. I immediately asked Mr. Shaw to have the kindness to send me if possible the pamphlet of Mr. Charles Bell, in order that I might render him all the justice that was his due. A few days afterwards I received it from Mr. Shaw.

This pamphlet is entitled:

Idea of a new anatomy of the brain, submitted for the observations of his friends, by Charles Bell, F.R.S.E. It is very curious, inasmuch as there is to be found in it the germ of the recent discoveries of the author in the nervous system. At page 22, the passage indicated by Shaw is to be found: I shall transcribe the whole of it.

"Next considering that the spinal nerves have a double root, and being of opinion that the properties of the nerves are derived from their connections with the parts of the brain, I thought that I had an opportunity of putting my opinion to the test of experiment, and of proving at the same time that nerves of different endowments were in the same cord and held by the same sheath.

"On laying bare the roots of the spinal nerves, I found that I could cut across the fasciculus of nerves, which took its origin from the posterior portion of the spinal marrow, without convulsing the muscles of the back; but that on touching the anterior fasciculus with the point of a knife, the muscles of the back were immediately convulsed."

It is seen by this citation of a work which I could not know, since it had not been published, that Mr. Bell, conducted by his ingenious ideas on the nervous system, was very near discovering the functions of the spinal roots; at the same time, the fact that the anterior are destined to motion, whilst the posterior belong more especially to sensation, appears to have escaped him: it is then to the establishment of this fact in a positive manner that I must limit my pretensions.

HERBERT MAYO

Herbert Mayo (1796-1852), physiologist of the Middlesex Hospital, London, took the next step after Bell and Magendie toward clarifying the problem of reflex action. In his *Anatomical and physiological commentaries,* part I of which appeared in 1822, he described the functions of the nerves of the face, ascribing motor power to what is termed the VIIth and common sensibility to the Vth. This unfortunately formed the beginning of a bitter and tiresome controversy with Bell, who fancied that he had made the discovery in a paper that had appeared in 1821. As in the controversy with Magendie, it is clear to anyone who will read the evidence impartially that Bell had, in point of fact, just missed the discovery, and that Mayo really deserves the credit. In part II of his "Commentaries" in 1833, he found that a circumscribed segment of the brain composed of the optic tubercles and the crura sufficed to give the pupillary reflex when the stump of the optic nerve was irritated. The following passage contains Mayo's account of this discovery.[11]

It is clear that an influence, independent of the will, occasionally throws voluntary muscles into action, as appears in tetanus, and other spasmodic disorders; and is shown remarkably in the physiological experiment of irritating the skin on the lower extremities, after the division of the spinal cord in the back, when the occurrence of action limited to the muscles of the lower extremities evinces that a connexion exists, independently of the will, between sentient surfaces and the action of voluntary mucles. I have varied this experiment by dividing the spinal cord at once in the neck and in the back, upon which three unconnected nervous centres exist; and the division of the skin in either part (and especially at the soles of the feet in the two hinder portions) produces a convulsive action of the muscles in that part. The same influence may then possibly regulate the unconscious actions to which these remarks relate.

An influence may be propagated from the sentient nerves of a part to their correspondent nerves of motion, through the intervention of that part alone of the nervous centre, to which they are mutually attached. Thus in vertebral animals, in which alone the fact is questionable, when the spinal cord has been divided in two places, an injury of the skin of either region is followed by a distinct muscular action in that part. Again: if the brain is quickly removed from the head of a pigeon, leaving only the crura cerebri together with the tubercles and the second and third nerve, on pinching the second nerve, the iris contracts.

MARIE-JEAN-PIERRE FLOURENS

MARIE-JEAN-PIERRE FLOURENS (1794-1867), Professor of Comparative Anatomy at the University of Paris, who carried out a prolonged series of experiments on the central nervous system, analysed the functions of the cerebellum and gave a singularly lucid description of cerebellar ataxia, which would serve for any modern text-book. After describing in his book[12] the consequences of removal of the cerebellum in a large number of animals, he draws his conclusions concerning the normal functions of this organ. Below is a protocol of an experiment on a dog, followed by his general conclusions (based on observations of twenty-one animals of various species.) He also studied the effects of alcohol and various other drugs on locomotion and, as the final selection indicates, he concluded that alcohol acted specifically on the cerebellum.

---

[11] Mayo, H. *Anatomical and physiological commentaries,* No. II, 1823 (pp. 17, 138).

[12] Flourens, P. *Recherches expérimentales sur les propriétés et les fonctions du système nerveux, dans les animaux vertébrés.* Paris: Crevot, xxvi, 331 pp., 1824 (pp. 145-146; 148-149; 259; 261-262).

EXPERIMENT XVI. ON A DOG

I made a lesion in the cerebellum of a young and healthy dog by means of incisions which extended deeper and deeper. The animal gradually lost the power of ordered and regular movement, and when the mid-region of the cerebellum was reached he could only totter along with a zigzag motion. When he tried to go forward he would go back and when he wished to turn to left he would turn right. He made great efforts to move, but being unable to control them he would bound forward suddenly and fall over himself. If there were any obstacle in his way he was quite unable to avoid it, however hard he tried, and he knocked against objects on all sides although he could see and hear perfectly well; when irritated he tried to bite and indeed did bite whatever was annoying him, if he could get hold of it, which was seldom, since he could not control his movements with precision. The animal was in full possession of his intellectual facilities and his senses and there was no trace of convulsion; he was merely deprived of the power to control and regulate his movements. When I extended the lesion to the inmost layer of the cerebellum the animal lost the power of motion and of equilibrium completely.

* * * * * *

I shall not add any further experiments here since the absolute similarity of those which have just been described make it unnecessary to do so. Thus 1. A slight injury to the cerebellum invariably produces a corresponding derangement of the power of motion in animals of all ages which increases in proportion to the injury; while complete removal of the cerebellum always causes total loss of the power of regulating movement.

2. At the same time there is a curious fact to be noted about the absolute regularity and repetition of these phenomena, *i.e.* in different animals the movements which are affected by [injury to] the cerebellum invariably correspond to their dominant type of movement. In birds which fly a great deal this derangement is particularly evident in their flight; it affects the gait of those which usually walk; and impedes swimming in birds accustomed to water.

There is therefore a drunken way of swimming and of flying, just as there is a drunken gait, and though the dominant means of progression may be impaired it still prevails.

3. Although removal of the cerebellum invariably coincides with loss of the power of locomotion, the intellectual faculties and the senses are not affected and so long as the operation is confined to the cerebellum there is no sign of convulsions.

The faculty which controls convulsions or muscular contraction, that which coördinates such contractions, and the faculties of the intellect and of the senses are therefore of three essentially different orders and reside in three separate regions of the nervous system.

4. Although with removal of the cerebellum an animal can no longer control its movements or maintain its balance when walking or standing, it still attempts to do so, and though it has lost the power of locomotion it can still move in self-defence.

This tendency to control balance and these movements in self-defence are therefore not derived from the cerebellum: it would be shown presently from whence they do proceed.

VI

EXPERIMENTS ON THE CEREBELLUM

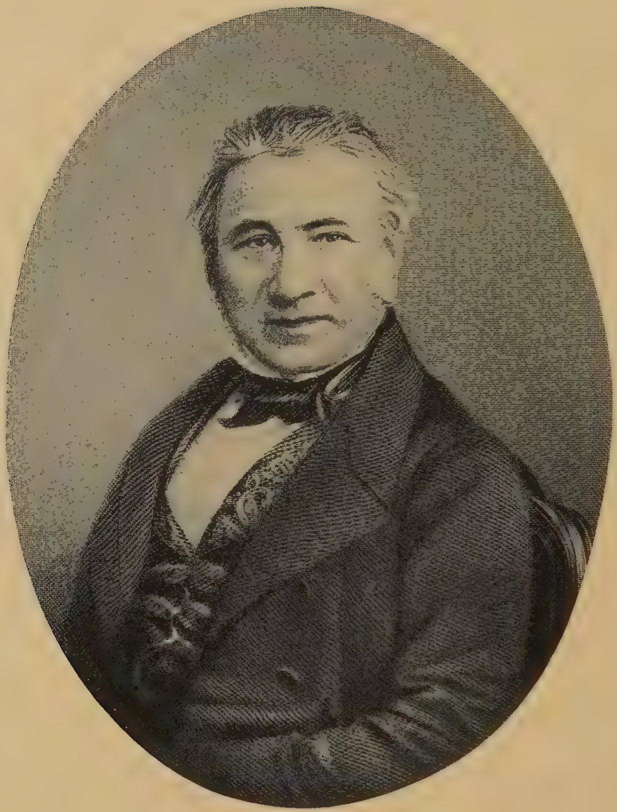
1. I caused a sparrow to swallow a few drops of alcohol and soon after it began to show signs of intoxication. It could only fly in a queer uncertain manner, wavering and twisting itself about in its flight, and when it walked it swayed about and described a zigzag course. After it had swallowed a few more drops (of alcohol) it could not even stand up or indeed stay in any fixed position. It behaved as though half the cerebellum had been removed after the first few drops and entirely removed after the final dose.

6. From these experiments it follows:

1 That a certain amount of alcohol acts exclusively and positively on the cerebellum.

2 That in acting thus exclusively, or, if you prefer it, specifically, on the cerebellum it affects only those functions which in previous experiments I have shown to proceed solely and specifically from that organ.

3 That if this amount is exceeded the action of the alcohol extends beyond the cerebellum.



Very truly yours
Marshall Hall

FIGURE 57. Marshall Hall (1780-1857) (from the engraved frontispiece to the *Memoirs of Marshall Hall* by his widow. London: 1861).

4 That the action of alcohol always leaves behind it traces which can be recognised and verified.

5 That especially in small birds, the formation and development of these traces are visible to the naked eye.

MARSHALL HALL

Marshall Hall (1790-1857), neurologist and indefatigable experimenter, who introduced the conception that the spinal cord is a chain of segments whose functional units are separate reflex arcs, added great impetus to the study of experimental neurology. He was one of the first, after Whytt, to attempt systematic correlation of clinical and experimental observations upon the nervous system. Hall was largely unaware of the work of his predecessors and it is to his credit that, beginning as it were *de novo,* he was able to travel as far as he did. In his important paper read to the Royal Society in 1833, he demonstrated tonic closure of the sphincters by reflex action, cessation of strychnine convulsions after destruction of the spinal cord and that most reflexes were more readily elicited by stimulating appropriate end-organs than through their bared nerve trunks. Several papers embodying his observations were published shortly before his memoir had been read to the Royal Society. Shortly after this paper appeared, Hall was denounced as a propagator of absurd and idle theories and, despite the enthusiastic reception of his work abroad, the *Philosophical Transactions* became from that time on closed to him as a channel of publication.

The first passage is from one of the preliminary descriptions of his experiments.[13]

THESE MOTIONS INDEPENDENT OF SENSATION AND VOLITION

A PAPER was read, containing "a brief account of a particular function of the nervous system," in which Dr. Marshall Hall detailed a series of experiments tending to prove the existence of *a source of muscular action distinct from all those hitherto noticed by physiologists, viz. volition, the irritation of the motor nerves in some part of their origin or course, or that of the muscles themselves.* The peculiarity of this motion he stated to consist in its being excited by irritation of the extreme portion of the sentient nerves, whence the impression is conveyed through the corresponding portion of brain and spinal marrow as a centre, to the extremities of the motor nerves. . . . .

The animals experimented on were salamanders, frogs and turtles.

---

[13] Hall, M. "These motions independent of sensation and volition." *Proc. Zoological Soc.,* Nov. 27, 1832.

In the first of these, the tail, entirely separated from the body, moved as in the living animal, on being excited by the point of a needle passed lightly over its surface. The motion ceased on destroying the spinal marrow within the caudal *vertebræ.* The head of a frog having been removed, and the spine divided between the third and fourth *vertebræ,* an eye of the separated head was touched: it was retracted and the eye-lid closed,—a similar movement being observed in the other eye. On removing the brain, these phenomena ceased. On pinching the skin, or the toe of one of the anterior extremities, the whole of this portion of the animal moved. On destroying the spinal marrow, this phenomenon also ceased. Precisely similar effects were observed on pinching the skin or toe of one of the posterior extremities; and on removing the last portion of the spinal marrow, this phenomenon ceased. The head of the turtle continues to move long after its separation from the body: on pinching the eye-lid, it is forcibly closed, the mouth is opened, and the membrane expanded under the lower jaw descends as in respiration. On pinching any part of the skin of the body, extremities, or tail, the animal moves. The posterior extremities and tail being separated together, the former were immovable; the latter moved on the application of the flame of a lighted taper to the skin. Those extremities had no connection with the spinal marrow. All movement ceased in the tail also, on withdrawing the spinal marrow from its canal.

'Three things,' Dr. Hall observes, 'are plain from these observations: 1. That the nerves of sensibility are impressible in portions of an animal separated from the rest; in the head, in the upper part of the trunk, in the lower part of the trunk: 2. that motions similar to voluntary motions follow these impressions made upon the sentient nerves: and 3. that the presence of the spinal marrow is essential as the central and cementing link between the sentient and motor nerves.'

The following passage is taken from the *Philosophical Transactions.*[14]

This animal was decapitated in the manner usual with cooks, by means of a knife, which divided the second and third vertebra.

The head being placed upon the table for observation, it was first remarked that the mouth opened and shut, and that the submaxillary integuments descended and ascended, alternately, from time to time, replacing the acts of respiration. I now touched the eye or eyelid with a probe. It was immediately closed: the other eye closed simultaneously. I then touched the nostril with the probe. The mouth was immediately opened widely, and the submaxillary membranes descended. This effect was especially induced on touching the nasal fringes situated just within the anterior part of the maxilla. I passed the probe up the trachea and touched the larynx. This was immediately followed by a forcible convulsive contraction of the muscles annexed to it. Having made and repeated these observations, I gently withdrew the medulla and brain. All the phenomena ceased from that moment. The eye, the nostril, the larynx were stimulated, but no movement followed.

---

[14] Hall, M. "The reflex function of the medulla oblongata and the medulla spinalis." *Phil. Trans.,* The Royal Society, 1833, pp. 635-665 (pp. 644, 650-651).

The next observations were made upon the other parts of the animal. The limbs, the tail, were stimulated by a pointed instrument or a lighted taper. They were immediately moved with rapidity. The sphincter was perfectly circular and closed; it was contracted still more forcibly on the application of a stimulus. The limbs and the tail possessed a certain degree of firmness or tone, recoiled on being drawn from their position, and moved with energy on the application of the stimulus. On withdrawing the spinal marrow gently out of its canal, all these phenomena ceased. The limbs were no longer obedient to stimuli, and became perfectly flaccid, having lost all their resilence. The sphincter lost its circular form and its contracted state, becoming lax, flaccid, and shapeless. The tail was flaccid, and unmoved on the application or stimuli.

It is distinctly proved, by this series of observations, that the reflex function exists in the medulla independently of the brain; in the medulla oblongata independently of the medulla spinalis; and in the spinal marrow of the anterior extremities, of the posterior extremities, and of the tail, independently of that of each other of these parts, respectively.

There is a still more interesting and satisfactory mode of performing the experiment: it is to divide the spinal marrow between the nerves of the superior and inferior extremities. We have then two modes of animal life: the first being the assemblage of the voluntary and respiratory powers with those of the reflex function and irritability; the second, the two latter powers only: the first are those which obtain in the perfect animal, the second those which animate the foetus. The phenomena are precisely what might have been anticipated. If the spinal marrow be now destroyed, the irritability alone remains—all the other phenomena having ceased.

The spinal marrow of a frog was divided between the anterior and posterior extremities. It was immediately observed that the head and the anterior extremities alone were moved spontaneously and with design, the respiration being performed as before. But the posterior extremities were not paralysed: they were drawn upwards, and remained perfectly motionless, indeed, unless stimulated; by the application of any stimulus, they were moved with energy, but once only, and in a manner perfectly peculiar. The stimulus was not felt by the animal, because the head and anterior extremities remained motionless at the time it was applied. Nothing could be more obvious, and indeed striking, than the difference between the phenomena of the functions of sensation and volition observed in the anterior part of the animal, and those of the reflex function in the posterior: in the former there were spontaneous movements with obvious design; in the latter, the mere effect of stimulus.

JOHANNES MÜLLER

Johannes Müller (1801-1858), the founder of the great German school of physiology in the 19th century made, like Malpighi and Haller, distinguished contributions to many branches of biological thought. His text-book (1834-1840) served to crystallize knowledge of the day and it stimulated work in almost every field. Müller, had he not been a physiologist, might have been the leading neurologist of his day. His penetrating analysis of experimental work on the nervous system, as exemplified in his text-book and in his numerous other writings, can still be read with profit today. He interested himself also in psychology and it was in his attempt to analyse sensation that he enunciated the principle which since 1826 has rightly borne his name. Müller's law of specific nerve energies gives expression to the fact that each sense organ, however it may be stimulated, gives rise to its own characteristic sensation and to no other: electrical stimulation of the optic nerve, for example, causes a sensation of light and nothing else. Though this generalization was set forth as early as 1826,[15] the principle is stated in somewhat more mature form in his text-book from which the following selection is taken.[16]

Section IV

OF THE PECULIAR PROPERTIES OF INDIVIDUAL NERVES

CHAPTER I

Of the nerves of special sense

The nerves have always been regarded as conductors, through the medium of which we are made conscious of external impressions. Thus the nerves of the senses have been looked upon as mere passive conductors, through which the impressions made by the properties of bodies were supposed to be transmitted unchanged to the sensorium. More recently, physiologists have begun to analyse these opinions. If the nerves are mere passive conductors of the impressions of light, sonorous vibrations, and odours, how does it happen that the nerve which perceives odours is sensible to this kind of impressions only, and to no others, while by another nerve odours are not perceived: that the nerve which is sensible to the matter of light, or the luminous oscillations, is insensible to the vibrations of sonorous bodies; that the auditory nerve is not sensible to light, nor the nerve of taste to odours; while, to the common sensitive nerve, the vibrations of bodies give the sensation, not of sound, but merely of tremours? These considerations have induced physiologists to ascribe to the individual nerves of the senses a special sensibility to certain impressions, by which they are supposed to be rendered conductors of certain qualities of bodies, and not of others.

---

[15] Müller, J. *Ueber die phantastischen Gesichtserscheinungen.* Coblenz: Jacob Hölscher, 1826. And *Zur vergleichenden Physiologie das Gesichtssinnes.* Leipzig: 1826.

[16] From Baly's English translation of Müller's *Handbuch* which appeared under the title of *Elements of physiology.* London: printed for Taylor and Walton, 2 vols., i-xxii+1-848 pp., 1838; xxii-xxxviii+849-1715+22. pp. 1842 (pp. 766-767).

This last theory, of which ten or twenty years since no one doubted the correctness, on being subjected to a comparison with facts, was found unsatisfactory. For the same stimulus as electricity, may act simultaneously on all the organs of sense,—all are sensible to its action; but the nerve of each sense is affected in a different way, becomes the seat of a different sensation: in one, the sensation of light is produced; in another, that of sound; in another, taste; while, in a fourth, pain and the sensation of a shock are felt. Mechanical irritation excites in one nerve a luminous spectrum; in another, a humming sound; in a third, pain. An increase of the stimulus of the blood causes in one organ spontaneous sensations of light; in another, sound; in a third, itching, pain, &c. A consideration of such facts could not but lead to the inference that the special susceptibility of nerves for certain impressions is not a satisfactory theory, and that the nerves of the senses are not mere passive conductors, but that each peculiar nerve of sense has special powers or qualities which the exciting causes merely render manifest.

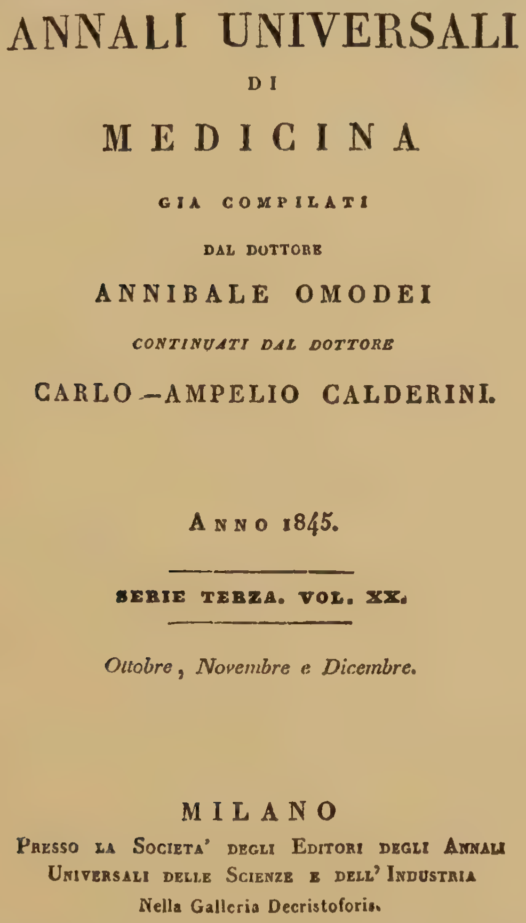
Sensation, therefore, consists in the communication to the sensorium, not of the quality or state of the external body, but of the condition of the nerves themselves, excited by the external cause.—We do not feel the knife which gives us pain, but the painful state of our nerves: the probably mechanical oscillation of light is itself not luminous; even if it could itself act on the sensorium, it would be perceived merely as an oscillation; it is only by affecting the optic nerve that it gives rise to the sensation of light: sound has no existence but in the excitement of a quality of the auditory nerve; the nerve of touch perceives the vibration of the apparently sonorous body as a sensation of tremour. We communicate, therefore, with the external world merely by virtue of the states which external influences excite in our nerves.

By the knowledge of the fact just announced, we are led not only to recognize the peculiar qualities of the different nerves of sensation, in addition to their general distinction from the motor nerves; but we are also enabled to banish for ever from the doctrines of physiology a number of erroneous notions regarding the supposed power of the nerves to perform the functions of each other. It has been long known that blind persons cannot recognize colours with their fingers, *as colours*; but we perceive now why it is impossible for them to do so; and the facts which show us the impossibility of it, afford an explanation of many other circumstances. However acute the sense of touch in the finger of the blind may be rendered by practice, it can be but the one sense proper to the nerves of the fingers,—*touch.*

ERNST HEINRICH WEBER AND EDUARD FRIEDRICH WEBER

Ernst Heinrich Weber (1795-1878), and his brother Eduard Friedrich Weber (1806-1871), both of Leipzig, shared the discovery of the inhibitory power of the vagus nerves upon the beating of the heart. Wilson-Philip (1826) had seen the heart lie "quite still for half a minute" after crushing the brain [see above, p. 88] and concluded that the brain controls the heart, but he did not discover the channels by which this control was exerted. Similarly, Alfred Wilhelm Volkman (1800-1877), the physiologist of Halle, had in 1837 actually observed inhibition of the heart on vagal stimulation, but being convinced that excitation of nerve always provoked increased activity of the tissue it innervates, he dismissed this chance observation as due to some error of technique. The Webers induced inhibition at first by connecting one pole of an electro-magnetic apparatus to the nostril of a frog and the other to the mid-region of the spinal cord, and they deserve great credit for finally tracing the pathway of the effect which they observed to the vagus. They extended their observations to include not only frogs, but also fish, birds, cats, dogs and rabbits. At first they believed that both vagi were necessary, but this view they soon abandoned. The experiment is a very important milestone in the history of physiology not merely because of its significance to the circulation, but because it brought to light a wholly new kind of nervous action and it formed the beginning of a series of highly significant researches upon the inhibitory processes occurring within the central nervous system. The discovery of the Webers, which was first communicated to a scientific congress meeting at Naples in September, 1845, was published in November of the same year in an obscure Italian medical journal edited by

Annibale Omodei.[17] The first page of the journal is reproduced in fig. 58. The following translation has been made from the original brief account in



ANNALI UNIVERSALI
DI
MEDICINA
GIA COMPILATI
DAL DOTTORE
ANNIBALE OMODEI
CONTINUATI DAL DOTTORE
CARLO-AMPELIO CALDERINI.

Anno 1845.

SERIE TERZA. VOL. XX.

Ottobre, Novembre e Dicembre.

MILANO
Presso la Societa' degli Editori degli Annali
Universali delle Scienze e dell' Industria
Nella Galleria Decristoforis.

FIGURE 58. The title-page of Omodei's *Annali* which contained the announcement of the Webers of the inhibitory action of the vagus.

Omodei's 'Annali,' and as far as I am aware it is the first time that it has been rendered into English.

---

[17] Weber, E. F. and E. H. Weber. "Experimenta, quibus probatur nervos vagos rotatione machinæ galvano-magneticæ irritatos, mortum cordis retardare et adeo intercipere." *Annali Universali di Medicina* (compilati dal A. Omodei), vol. 116, Fasc. 347 (Ser. 3, vol. 20), pp. 227-228, Milan, Nov., 1845. In January, 1846, this paper was reprinted in Mandl's *Archives d' Anatomie générale et de Physiologie* (the title borne by a supplementary volume to *Arch. gén. de Med.*, 4ième Sèr., for 1846). The experiments were described in greater detail on pages 42-48 and on p. 120 of an article entitled "Muskelbewegung" which Eduard Weber contributed to Rudolph Wagner's *Handwörterbuch der Physiologie,* Bd. 3, pp. 1-122, 1846. The translation given below has been made from the original text in the Italian journal.

THE EXPERIMENTS OF *EDWARD* AND *ERNEST HENRY WEBER* BY WHICH IT IS PROVED THAT WHEN STIMULATED WITH A ROTARY ELECTROMAGNETIC APPARATUS THE VAGUS NERVES SLOW DOWN AND, TO A CONSIDERABLE EXTENT, INTERRUPT THE HEART-BEAT

I. If the medulla oblongata of a frog or the ends of the isolated vagus nerves are excited by the rotation of a fairly strong electromagnetic machine, the heart suddenly stops beating, but at the end of excitation begins after a short interval to beat again: at first slowly and weakly, then gradually more strongly and more frequently until finally the original beat observed before excitation is restored.

II. The rotation of a less powerful instrument slows down and weakens the heart-beat. The heart, whose beat is by this means interrupted, is not contracted as in a tetanic convulsion, but remains relaxed and has a flat appearance.

III. The excitation of the vagus nerve on one side only does not change the heart-beat.

If excitation of the vagus nerves is continued long enough for the force producing their excitation to be exhausted, the heart begins to beat again.

IV. If the adjacent parts of the heart in which the sympathetic nerves run or extend their branches, are excited in the same way, the heart-beats, so far from stopping or slowing down, rather become more frequent and, if they had previously been stopped, are restored.

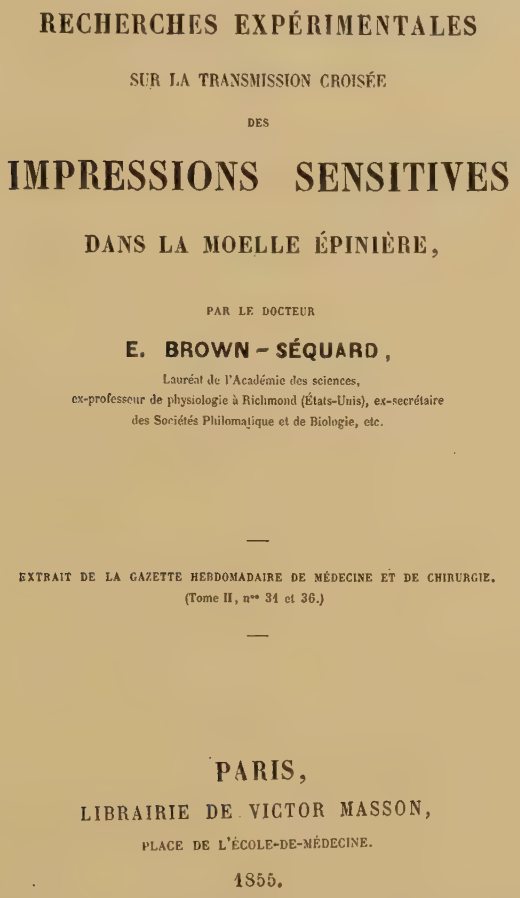
V. But it is uncertain whether this effect depends more on the excitation of the sympathetic nerve than on the electricity directly spreading to the heart by means of the moist animal tissue.

VI. If the wire connection from the electromagnetic machine is applied directly to the heart in a certain way, it can cause the heart to become contracted tetanically, and to cease to beat for as long as response lasts.

VII. The excitation of vagus nerves as described has an effect in rabbits similar to that in frogs.

C. E. BROWN-SÉQUARD

C. E. Brown-Séquard (1817-1894), the first to point out the clinical significance of experimental hemisection of the spinal cord, had a meteoric career. Born in Mauritius of a French mother and an American father, he moved from place to place expending his phenomenal abilities in the most diverse ways. Poverty-stricken, and given to free expression of radical political views, he was forced, in 1852, to leave France for America, where he supported himself in New York by the practice of obstetrics and charged $5 a case for his services. He returned to France, but in 1855 one finds him once more in America, this time teaching the "institutes" of medicine at Virginia Medical College. Later



RECHERCHES EXPÉRIMENTALES
SUR LA TRANSMISSION CROISÉE
DES
IMPRESSIONS SENSITIVES
DANS LA MOELLE ÉPINIÈRE,

PAR LE DOCTEUR
E. BROWN-SÉQUARD,
Lauréat de l'Académie des sciences,
ex-professeur de physiologie à Richmond (États-Unis), ex-secrétaire
des Sociétés Philomatique et de Biologie, etc.

—

EXTRAIT DE LA GAZETTE HEBDOMADAIRE DE MÉDECINE ET DE CHIRURGIE.
(Tome II, nos 31 et 36.)

—

PARIS,
LIBRAIRIE DE VICTOR MASSON,
PLACE DE L'ÉCOLE-DE-MÉDECINE.
1855.

FIGURE 59. The title-page of Brown-Séquard's paper on the crossing of sensory tracts in the spinal cord (obtained through the courtesy of the Royal Society).

(1864-67) he occupied the Chair of Physiology and Pathology of the nervous system at Harvard. Following the death of Claude Bernard in 1878, he became his successor as Professor of experimental medicine in the Collège de France. His observations on the physiology of the spinal cord were carried out over a long period and were published at intervals in the *Comptes Rendus,* from 1849. It is true that his views were to some extent modified, but the salient points which he emphasized have stood unchallenged. The first two paragraphs below[18] are taken from his lectures on this subject to the Royal College of Surgeons, delivered in May, 1858. As the third paragraph shows,[19] Brown-Séquard deserves great credit also for his observations upon the effects of stimulation of the cervical sympathetic, a discovery made independently by Claude Bernard.

It seems absolutely certain, from the above facts and reasonings, that there is no decussation of the voluntary motor fibres of the trunk and limbs above the crossing of the pyramids. On the other hand, we have already shown, in a previous lecture, that there seems to be no decussation of these fibres in the spinal cord—*i.e.,* below the crossing of the pyramids; so that we are led to admit that most of, if not all, the conductors of the orders of the will to muscles decussate at the lower part of the medulla oblongata, and that these conductors chiefly form the anterior pyramids, after their decussation. An interesting fact, in addition to those already mentioned, concerning these pyramids, is, that when a lesion exists at the place of decussation, it produces a paralysis in the two sides of the body, because it destroys fibres belonging to them both. This is a feature quite peculiar to this part of the cerebro-spinal axis.

From the preceding remarks, and from the facts and reasonings contained in our lectures (the third and seventh) on the decussation of the conductors of sensitive impressions, it results that, as regards anæsthesia and paralysis, three different groups of symptoms may be observed, according to the place of the alteration in a lateral half of the cerebro-spinal axis: 1st, above the decussation of the pyramids, a lesion on either the medulla oblongata, the pons Varolii, the crura cerebri, the optic thalami, the corpora striata, or the brain proper, if it produces anæsthesia and paralysis, produces them both in the opposite side of the body; 2d, below the decussation in the pyramids, a lesion in the spinal cord produces paralysis in the same side, and anæsthesia in the opposite side; 3d, at the level of the decussation of the pyramids, and upon the decussating fibres, and also behind them, a lesion produces paralysis in both sides of the body, and anæsthesia only in the opposite side. So that wherever the lesion, in a lateral half of the cerebro-spinal axis, may be—below, above, or at the level of the crossing of the pyramids—if it produces anæsthesia, it is in the opposite side; while paralysis, in these three cases, is either in the same or the opposite side, or in both sides.

---

[18] Brown-Séquard, C. E. *Course of lectures on the physiology and pathology of the central nervous system.* Philadelphia: Collins, xii, 276 pp., 3 plates, 1860 (pp. 199-200). His original papers describing the consequences of hemisection of the spinal cord are numerous. The most important is the following: "Explication de l'hemiplégie croisée du sentiment." *Comp. Rend.,* 1850, pp. 70-73; see also *ibid.,* pp. 134 and 195 and *Récherches expérimentales sur la transmission croisée des impressions dans la moelle épinière.* Paris: Victor Masson, 1855, which is reproduced in fig. 59.

* * * * * *

I[19] have found that the remarkable phenomena which follow the section of the cervical part of the sympathetic, are mere consequences of the paralysis and therefore of the dilatation of the blood-vessels. The blood finding a larger way than usual, arrives there in greater quantity; therefore the nutrition is more active. Now the sensibility is increased because the vital properties of the nerves are augmented when their nutrition is augmented . . . . I base my opinion in part on the following experiments: If galvanism is applied to the superior portion of the sympathetic after it has been cut in the neck, the vessels of the face and of the ear after a certain time begin to contract; their contraction increases slowly, but at last it is evident that they resume their normal condition, if they are not even smaller. Then the temperature and the sensibility diminish in the face and in the ear, and they become in the palsied side the same as in the sound side. When the galvanic current ceases to act, the vessels begin to dilate again, and all the phenomena discovered by Dr. Bernard reappear.

DAVID FERRIER

Sir David Ferrier (1843-1928), the English neurologist, laid the foundation of knowledge concerning the localization of cerebral function. Fritsch and Hitzig had, by galvanic stimulation, defined the motor area of the brain. Goltz had described the gross results of extirpation of the posterior half, and the anterior half respectively, of the cerebral hemispheres of dogs, but he denied that there was localization of function. Ferrier, through the study of experimental and of clinical evidence, allocated certain well-recognized functions to specific areas of the hemispheres; as Sherrington[20] has said: "He established the localization of the 'motor' cortex very much as we now know it. He located it as a region accompanying the Rolandic fissure across the lateral aspect of the hemisphere and extending thence over and upon the hemisphere's median aspect. He pointed out that its extent was greater and its character more detailed in the ape than in any of the types less near to man. He showed that its focal movements were obtainable with such definition and precision that 'the experimenter can predict with certainty the result of stimulation of a given region.' He went on to determine the effects of destruction of limited portions of the cerebral cortex. He allocated regions specially concerned with vision and with hearing respectively. He showed that the hemiplegias and monoplegias, ensuing on injuries within the motor region of the ape, were characteristically greater than those produced by similar cerebral lesions in the dog. The symptoms in the ape he stressed as being strikingly akin to those familiar in the clinic. At the International Congress of Medicine of 1881, held in London, he gave a convincing demonstration of his results before a gathering of the neurologists of Europe. Sir Charles Ballance, who was present, relates that on the appearance of one of Ferrier's hemiplegic monkeys, the clinician Charcot, of Paris, exclaimed 'It is a patient!' —words pregnant as a pronouncement on the case for which Ferrier was arguing." Ferrier had begun his studies on the cortex cerebri in 1873 and the results of his first experiments were published in the *Reports* of the West Riding Asylum where he had worked. In 1874 and 1875 appeared his two Croonian Lectures and in 1876 his celebrated book *The functions of the brain,*[21] from which the following passage is taken.

---

[19] Brown-Séquard, C. E. "Experimental researches applied to physiology and pathology." *Medical Examiner,* Philadelphia, vol. 8, pp. 481-504, 1852 (p. 486).

[20] Sherrington, C. S. "Obituary notice of Sir David Ferrier." *Proc. Roy. Soc.,* vol. 103B pp. viii-xvi, 1928 (p. x).

EXTIRPATION OF THE MOTOR CORTEX

The question, however, with which we are more particularly engaged is the determination of the physiological significance of these regions [pre-frontal convolutions]. The mere fact of the excitation of movements is, as we have already seen, no proof that the regions stimulated have a motor significance, for the stimulation of a sensory centre may give rise to reflex or associated movements. Whether the centres now under consideration are directly motor, or only give rise to movements in a reflex or indirect manner when stimulated, is a question which has been answered differently by different investigators on this subject. The definite purposive character clearly perceivable in many of the movements, and their correspondence with the ordinary volitional activities and peculiarities of the animals, apart from other considerations, point rather to the conclusion that they are the result of the artificial excitation of the functional activity of centres immediately concerned in effecting volitional movements, and as such truly motor. As the question, however, is one capable of being answered by direct experiments, we may proceed to the consideration of these. If these regions are centres of voluntary motion, paralysis of voluntary motion ought to follow from their destruction, and any apparent exception to this result must be capable of satisfactory explanation, consistently with this view, if it is the correct one.

---

[21] Ferrier, D. *The functions of the brain.* London: Smith, Elder and Co., xvi+323 pp. 1876, (pp. 200-203); 2nd ed., 1886.

The following experiments on monkeys give no uncertain reply to the questions stated.

The first experiment I have to record is instructive, as showing the respective effects of irritation and destruction of the convolutions bounding the fissure of Rolando. The right hemisphere of a monkey had been exposed and subjected to experimentation with electrical irritation. The part exposed included the ascending parietal, ascending frontal, and posterior extremities of the frontal convolutions. The animal was allowed to recover, for the purpose of watching the effects of exposure of the brain. Next day the animal was found perfectly well. Towards the close of the day following, on which there were signs of inflammatory irritation and suppuration, it began to suffer from choreic spasms of the left angle of the mouth and left arm, which recurred repeatedly, and rapidly assumed an epileptiform character, affecting the whole of the left side of the body. Next day left hemiplegia had become established, the angle of the mouth drawn to the right, the left cheek-pouch flaccid and distended with food, which had accumulated outside the dental arch; there being almost total paralysis of the left arm, and partial paralysis of the left leg. On the day following the paralysis of motion was complete over the whole of the left side, and continued so till death, nine days subsequently. Tactile sensation, as well as sight, hearing, smell and taste, were retained. On *post-mortem* examination it was found that the exposed convolutions were completely softened, but beyond this the rest of the hemisphere and the basal ganglia were free from organic injury.

In this we have a clear case, first, of vital irritation producing precisely the same effects as the electric current, and then destruction by inflammatory softening, resulting in complete paralysis of voluntary motion on the opposite side of the body, without affection of sensation.

In the next experiment the lesion was more limited, and the state of paralysis was limited correspondingly. The left hemisphere of a monkey was exposed, and the cortical substance destroyed by the cautery in the post-parietal lobule (foot-centre), ascending parietal convolution (hand and wrist movements), and superior part of the ascending frontal convolution (movements of arm and leg). The centres of the biceps, facial muscles, and mouth and tongue were not involved. Immediately on this being done the right leg was found to be dragged, the foot and ankle especially hanging flaccid and powerless.

The right hand and wrist hung powerless and flaccid, but the animal could flex the forearm and maintain resistance against extension, a fact easily accounted for by the biceps centre remaining intact. There was no trace of facial paralysis or distortion of the angle of the mouth. Cutaneous sensation and the various special senses were unimpaired, and beyond the paralysis mentioned the animal was in good condition, and enjoyed food. In this animal the angular gyrus was subsequently destroyed, with the effect of causing blindness of the right eye.

On *post-mortem* examination next day the lesion was found to occupy the motor regions specified and the angular gyrus, the rest of the brain and the basal ganglia being intact.

In this case the paralysis was confined to the same movements as a result from electric stimulation of the centres specified. In the following experiment the extent of the lesion was still further circumscribed, and the effect, as regards voluntary motion, correspondingly limited.

CHARLES SCOTT SHERRINGTON

Sir Charles Scott Sherrington, Waynflete Professor of Physiology at Oxford, has carried out a prolonged series of observations upon the central nervous system, which have had a profound influence upon modern physiological thought. Working always objectively, devising experiments, recording results and scrupulously avoiding speculation, he has accumulated a large body of facts which have been made the basis of a few far-reaching generalizations: levels of nervous integration, the final common path, the proprioceptive system, the nature of higher controlling centers such as the motor cortex, postural contraction (tonus), and the nature of central inhibition. The conception of the integrative functions of the nervous system was first set forth in 1906 under the auspices of the Silliman Lectureship at Yale.[22] The first quotation below[23] is taken from the *British Association Report* in which the principle of the final common path was first described. In the second selection[24] the original definition of the proprioceptive system is given. Probably the most important contribution in recent years from Sherrington's laboratory is the discovery of the stretch reflex which was made in collaboration with Liddell. It was found that the long debated problem of muscle tonus really resolved itself into an analysis of the response of muscles to stretch and that postural contraction is maintained chiefly through the stretch imposed upon antigravity muscles. Their conclusions are given in the third selection.

[22] Sherrington, C. S. *The integrative action of the nervous system.* New Haven: Yale University Press, xviii, 411 pp., 1906.

[23] Sherrington, C. S. "Correlation of reflexes and the principle of the common path." *Brit. Assn. Report,* pp. 1-14, 1904 (pp. 13-14).

[24] Sherrington, C. S. "On the proprioceptive system, especially in its reflex aspect." *Brain,* vol. 29, pp. 467-482, 1906 (pp. 468-469; 471-472).

CORRELATION OF REFLEXES AND THE PRINCIPLE OF THE COMMON PATH

The principle I have tried to outline to you has many and wide applications; it seems fruitful for problems of Pathology and Psychology, as well as for those of Physiology. But I keep you too long. Let me sum up. The reflex arcs (of the synaptic system) converge in their course so as to impinge upon links possessed by whole varied groups in common—*common paths.* This arrangement culminates in the convergence of many separately arising arcs upon the efferent-root neurone. This neurone thus forms a final common path for many different reflex arcs and acts. It is responsive in various rhythm and intensity, and is relatively unfatigable. Of the different arcs which use it in common, each can do so exclusively in due succession, but *different* arcs cannot use it simultaneously. There is, therefore, interference between the actions of the arcs possessing the common path, some reflexes excluding others and producing inhibitory phenomena, some reflexes reinforcing others and producing phenomena of 'bahnung.' Intensity of stimulation, species of reflex, fatigue, and freshness, all these are physiological factors influencing this interaction of the arcs—and under pathological conditions there are many others, e.g. 'shock,' toxins, &c. Hence follows successive interchange of the arcs that dominate one and the same final common path. We commonly hear a muscle—or other effector organ—spoken of as innervated by a certain nerve; it would be more correct as well as more luminous to speak of it as innervated by certain receptors; thus, the hip flexor, now by this piece of skin, now by that, by its own foot, by the opposite fore-foot, by the labyrinth, by its own muscle-spindles, by the eye, by the 'motor' cortex, &c. This temporal variability, wanting to the nerve-net system of medusoid and lower visceral life, in the *synaptic* system provides the organism with a mechanism for higher integration. It fits that system to synthesise from a mere collection of tissues and organs an individual animal. The animal mechanism is thus given solidarity by this principle which for each effector organ allows and regulates interchange of the arcs playing upon it, a principle which I would briefly term that of 'the interaction of reflexes about their common point.'

THE PROPRIOCEPTIVE SYSTEM

The receptor organs, if one regards their distribution from a broad point of view, fall naturally into two great groups, as judged by their locus in the body. They are distributed in two great separate fields, each field circumstanced fundamentally differently from the other. Multicellular animals, regarded broadly throughout a vast range of animal forms, are cellular masses which present to the environment a surface sheet of cells and, underneath that surface sheet, a bulk made up of cells more or less screened from the environment by the surface sheet overlying them. The surface sheet is directly exposed to the environment, and is adapted to react to many of the factors composing that environment, these factors constituting stimuli. Bedded in the surface sheet are numbers of receptor cells, developed in adaptation to the stimuli delivered by environmental agencies. Many of the agencies by which the environment acts on the organism do not, however penetrate to the mass of cells forming the organism's deeper parts. Thus various stimuli in the forms of light and heat, and localised pressures, and chemical substances expend themselves as stimuli at the surface sheet, and do not penetrate into the depth of the organism. But the deep tissues, although devoid of receptors adapted to these surface-reaching stimuli, are, nevertheless, not unprovided with receptors. They have receptors of other kinds apparently specific to them. Some agencies act not only at the surface of the organism, but also through its mass. For some of these agencies no receptors appear to be adapted; for instance, there seem to be none adapted for the Röntgen rays. For others of more common occurrence, receptors in the deep tissues seem to have been evolved. The deep receptors appear to be very usually adapted to mechanical stimuli of certain kinds. Thus they seem adapted to react to the compressions and strains produced by muscles, and an important adequate agent for them seems to be mass acting in the modes of weight and inertia, involving mechanical pressures and mechanical stresses.

The main fields of distribution of the receptor organs fundamentally distinguishable seem, therefore, to be two, namely, a *surface* field constituted by the surface layer of the organism and a *deep* field constituted by the tissues of the organism beneath the surface sheet.

But the surface field is further broadly subdivisible. Its subdivisions are two. Of these one lies freely open to the numberless vicissitudes and agencies of the environment; it is co-extensive with the so-called external surface of the animal. It is cutaneous in the widest sense of that term. It possesses as receptive organs not only those of touch, &c., in the skin proper, but also the eye, nose, and organ of hearing. This subdivision of the surface field contrasts with a second subdivision of it, constituted by what is commonly termed the internal surface of the animal, the alimentary or intestinal surface. This latter surface is, it is true, in contact with the environment; but the environment with which it is in contact is a portion of the environment greatly modified from the general environment outside by lying almost completely surrounded by the animal itself. This part of the receptive field of the animal's surface, which is turned inward upon the alimentary contents, may be termed the *intero-ceptive,* in contradistinction to that larger part of the surface field which looks outward upon the free environment in general, and the latter may from that circumstance be termed the animal's *extero-ceptive* surface. . . .

Returning to the receptor organs bedded in the deep tissues, and to the study of the reactions which they subserve, two characters attract attention as differentiating them from those of the surface field, whether extero-ceptive or intero-ceptive. Of these features, one is that the *stimuli* effective on the receptors of the deep field differ fundamentally from those operative on the receptors of either subdivision of the surface field. Most of the stimuli by which the external world commonly acts on the surface of the animal are excluded from the deep field. But the organism itself, like the external world surrounding it, is a field of ceaseless change where internal energy is continually being liberated, whence chemical, thermal, mechanical, and electrical effects appear. It is a microcosm in which forces which can act as stimuli are at work, in the microcosm around. The receptors which lie in the deep tissues appear adapted for excitation by changes going forward in the organism itself. These changes work, it appears, largely through the agency of mass with its mechanical consequences of weight and inertia, and also largely through mechanical strains and alterations of pressure resulting from contractions and relaxations of muscles. *Therefore, a character of the stimulations occurring in this deep field is that the stimuli are traceable to actions of the organisms itself,* and are so in much greater measure than are the stimulations of the surface field of the organism. Since in the deep field the stimuli to the receptors are delivered by the organism *itself* the deep receptors may be termed, *proprio-ceptors,* and the deep field a field of proprioception.

REFLEXES IN RESPONSE TO STRETCH (MYOTATIC REFLEXES)[25]

Familiar to those who work with the decerebrate preparation must be the observation that passive flexion of the characteristically extended knee is felt to evoke some development or resistance of it against that passive movement. Examination by the myograph of this resistance formed the point of departure of the following observations.

In this same muscle the "knee jerk" is doubtless a reflex in response to a stretch; but it is a reaction whose brevity makes it perhaps the most twitch-like of all reflexes, whereas the reflex under consideration here is tetanic and prolonged. Patellar-clonus, likewise a reaction to stretch, resembles a spaced series of knee jerks and, wanting tetanic character, likewise differs from the reflex under consideration here.

SUMMARY OF CONCLUSIONS

In the knee-extensor (decerebrate preparation) a stretch applied to the muscles evokes contraction in it. This is reflex and purely proprioceptive, its receptors lying in the fleshy region of the muscle. A stretch less in extent than .8 per cent. of the total muscle-length suffices to evoke the reflex. Slow stretches, *e.g.,* of 5 mm. performed in 6 sec., evoke the reflex as well as do quick. The latency of the reflex is short, *e.g.,* less than 20σ, but the lower limit of latency we have not determined.

Within limits, so long as the stretch increases, the reflex continues to increase. When augmentation of the stretch ceases, augmentation of the reflex contraction also ceases and the reflex usually declines, merging into long-lasting plateau-like contraction, which is maintained by the stretched-posture, consequent from the precurrent stretch-movement. Withdrawal of the stretch causes immediate cessation of this postural stretch contraction. The stretch-reflex unlike the ordinary contralateral extensor reflexes, therefore, exhibits little or no after-discharge, *i.e.,* the reflex is relatively dead-beat.

When the application of the stretch is confined to a portion only of the muscle, the reflex contraction is also confined to that portion.

The reflex is readily diminished and annulled by reflex inhibition provoked from the sources recognized as regularly inhibitory for the knee-extensor. Under this inhibition, the muscle's reaction to stretch resembles indistinguishably in our records that yielded by the muscle after complete paralysis from severance of its motor nerve. Similarly, after severance of the afferent nerve-fibres of the muscle the reaction of the muscle to stretch becomes indistinguishable from that of the inhibited or paralysed muscle, and no trace of reflex contraction in response to the stretch has been discoverable. Direct stimulation, electrical or mechanical, of the afferent nerve of a part of the muscle produces inhibitory relaxation of the stretch contraction in the other parts of the muscle, *i.e.* among receptors in the muscle, there are in addition to those excitable by stretch and provoking reflex contraction in the muscle, others which provoke reflex inhibition of the muscle.

---

[25] Liddell, E. G. T. and C. S. Sherrington. "Reflexes in response to stretch (myotatic reflexes)." *Proc. Roy. Soc.,* vol. 97B, pp. 212-242, 1924 (pp. 212; 241); pp. 267-283, 1925.

Post-inhibitory rebound is facilitated and augmented by stretch of the muscle; this is so even when the stretched-posture has been maintained for many minutes at the time when the post-inhibitory period occurs. Knee-jerk and patellar clonus seem to be fractional examples of the stretch-reflex.

Some application of the experimental results to the reflex co-ordination of standing and of locomotor acts is attempted.

HARVEY CUSHING

Harvey Cushing, the Moseley Professor of Surgery at the Harvard Medical School, has taken advantage of the exceptional opportunities which operations on the human brain have offered for analysis of function, especially when carried out under local anæsthesia (a procedure which he was the first to introduce). As a pupil in Sherrington's laboratory at Liverpool, he assisted in the experiments on stimulation of the motor area of the higher apes and soon afterwards he made corresponding observations on human beings under surgical anæsthesia. The story of his first experience in stimulating the motor and sensory areas of a conscious patient is told in the following passage.[26] The appeal of the human experiment is always great and it is particularly so in this instance, for it established convincingly that the reactions studied in higher apes were applicable to human beings and it provided for the first time direct evidence that irritation of the postcentral gyrus gives rise to sensation; a fact which could not be established by experiments on animals.

THE HUMAN MOTOR CORTEX

A year ago I reported, with Dr. H. M. Thomas, a surgical experience[27] in which at a second-stage operation an osteoplastic flap, previously made, was re-elevated, the dura reflected, the cortex incised, and a subcortical cystic tumour removed from the postcentral field of an unanæsthetized patient. The procedure, with the exception of accidental dragging upon the dura, and the final reclosure of the scalp, not only occasioned no discomfort, but was attended on the part of the patient by a lively and helpful interest in the performance. He even informed us of a focal sensory attack which occurred early in the proceedings, evidently incited by the preliminary palpation of the exposed brain.

---

[26] Cushing, H. "A note upon the faradic stimulation of the postcentral gyrus in conscious patients." *Brain,* vol. 125, pp. 1-5, 1909 (pp. 4-5; pp. 7-8; p. 11).

[27] "Removal of a subcortical cystic tumour at a second-stage operation without anaesthesia." *Jour. Amer. Med. Assoc.,* vol. 1, pp. 847-956, 1908.

In the past year, however, the exigencies of two surgical cases have given us the looked-for opportunity of making further observations upon the sensory field.

Operation (*second stage, July 6, 1908*).—After a preliminary injection of ⅛ gr. of morphia, and under primary anæsthesia by chloroform, the edges of the former incision were newly separated and the original bone-flap quickly re-elevated. The patient promptly regained complete consciousness, and while in this state, without occasioning discomfort, the dura was divided in the line of the previous closure, and the membrane was again reflected.

Cortical stimulation.—The following electrical observations were then made. The same movements as before were easily elicited with a mild faradic current from the precentral strip. These motor responses in detail and in the order in which they were obtained from the areas shown in the accompanying sketch (fig. 60) consisted of:—

(1) An opposing movement of thumb and fingers from points opposite to the unmistakable genu.

(2) Somewhat higher up, extension of the index finger.

(3) Still higher flexion of the fingers, which carried over to flexion of the wrist.

(4) At the upper margin of the exposed field, flexion of the elbow.

(5) Below the evident middle genu the movements, which required a somewhat stronger current, consisted of contraction of the side of the face.

(6) Movements of palate and fauces, a curious choking sensation being occasioned whenever they were obtained; and

(7) From the very lowest exposed part of the strip movements of the tongue occurred, and the patient experienced a sensation of movement in the lower jaw, though this was not certified by the observers.

It is to be noted that the subject was perfectly aware of these movements, and in the attempt to express the sense of feeling which was occasioned by them he said that it was the same sort of a drawing sensation appreciated when the muscles are "pulled" by peripheral stimulation—a familiar experience for him, owing to a long course of electrical treatment before his admission to the hospital. The movements, in other words, gave him the sensation of active muscular contraction alone.

Posterior to the central fissure, over an area roughly corresponding with the upper two-thirds of the exposed postcentral convolution (fig. 60), stimulation, with the same strength of current used to elicit the motor responses from the precentral gyrus, led to a sensation in the hand, arm and little finger—chiefly in the little finger—which was said to be exactly akin to the sensation that inaugurated his attacks. Stimulation lower down on the postcentral gyrus occasioned a sensation of warmth in the arm, but this was rather vague and indescribable.

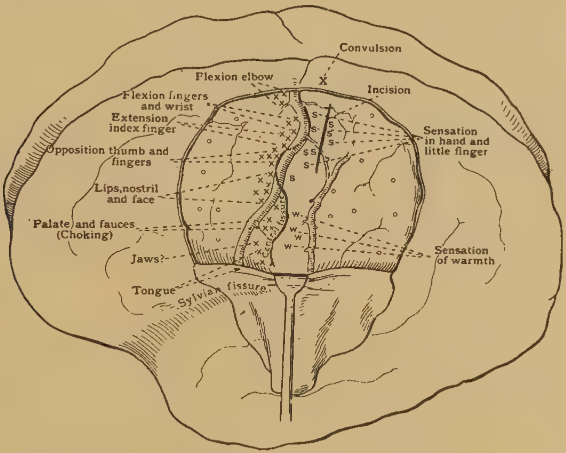

Convulsion
X
Flexion elbow
Incision
Flexion fingers and wrist
Extension index finger
Opposition thumb and fingers
Lips, nostril and face
Palate and fauces (Choking)
Jaws?
Tongue
Sylvian fissure
Sensation in hand and little finger
Sensation of warmth

FIGURE 60. The motor and sensory areas as first delineated experimentally by Cushing in a conscious human being (*Brain,* 1909, vol. 125, p. 6).

It is to be noted that there were no painful sensations whatsoever, and further, that stimulation of the field in front of the motor strip and back of the postcentral convolution elicited no movements or sensations whatsoever, and the patient seemed to be unaware of the application of the electrode.

On elevating the upper edge of the dura at the point X (fig. 60) and placing the electrode there, an attack precisely similar to his usual attacks, inaugurated by the same sensory disturbances and followed by the customary abduction of the arm and arching of the body to the side, was produced. This lasted but a few moments, and was not followed by a general convulsion nor by loss of consciousness.

COMMENT

These observations seemingly add confirmation to the view which ascribes a sensory function to the gyrus centralis posterior, but beyond this I shall make no endeavour to interpret their significance. Just what relation the afferent impulse bears to a motor response; just how stimulation of this supposedly sensory field is interpreted by the subject as sensory; why the motor response from stimulation of the gyrus centralis anterior occurs without any primary afferent impression, but only with the secondary consciousness of the movement—these and many other questions that arise are matters rather for the psychologist.

It is, perhaps, noteworthy that the sensations which were obtained were limited entirely to the hand and arm; and whether this means that there is an especially wide cortical representation for afferent impulses from this region, or whether these patients, owing to the characteristics of their seizures, possessed sensory centres from hand and arm which were unduly excitable, is difficult to tell, and will need further elucidation.

RUDOLPH MAGNUS

Rudolph Magnus (1872-1927), for many years the Professor of Pharmacology at Utrecht, set himself the problem of turning anatomical facts concerning the nervous system into physiological language. His investigations in this field of work were commenced in 1908 after spending a winter in Sherrington's laboratory at Liverpool and they culminated in 1924 in a now classical monograph on animal posture.[28] During that interval nearly 150 papers on the physiology of posture had come from his laboratory. Magnus had the happy faculty of being able to describe with astonishing clearness, even in a tongue that was not his own, reactions occurring in three dimensions of space. This is nowhere better illustrated than in his Croonian Lecture from which the following passage is taken.[29]

Animal Posture.—Every movement starts from and ends in some posture, so that I think a discussion of "Animal Posture" falls well within the scope of the intention of Dr. William Croone, when he founded these annual Lectures to promote the study of "Muscular Motion." Before beginning I wish to emphasize how greatly I appreciate the honour of delivering before you this Lecture, and how I especially enjoy the pleasure of doing so with Sir Charles Sherrington in the Chair, who long ago took the trouble to introduce me to his beautiful methods of investigating the central nervous system, and to allow me an insight into his fruitful views on the function of nervous centres.

---

[28] Magnus, R. *Körperstellung.* Berlin: Springer, xiii+740 pp., 1924.

[29] Magnus, R. "Animal posture." Croonian Lecture. *Proc. Roy. Soc.,* vol. 98B, pp. 339-353, 1925.

As it is impossible to consider the whole problem of posture in one short lecture, I propose to speak to you to-day on four partial problems, which are closely connected with each other, and which provided the starting points for investigations which have been carried out in my laboratory at Utrecht, with the aid of a great number of able collaborators. These partial problems are:—

1. *Reflex standing.*—In order to carry the weight of the body against the action of gravity, it is necessary that a certain set of muscles, the "standing muscles," should have by reflex action a certain degree of enduring tone, to prevent the body from falling down on the ground.

2. *Normal distribution of tone.*—In the living animal not only do these standing muscles possess tone, but also the other muscles of the body, especially their antagonists, *i.e.* the flexors. Between these two sets of muscles a certain balance of tone exists, so that neither set of muscles gets too much or too little tone.

3. *Attitude.*—The position of the different parts of the body must harmonise with each other; if one part of the body be displaced, the other parts also change in posture, so that different well-adapted attitudes, evoked by the first displacement, will result.

4. *Righting function.*—If by its own active movements or by some outside force the body of an animal is brought out of the normal resting posture, then a series of reflexes are evoked, by which the normal position is reached again.

The main *centres* for all those four functions are situated in close neighbourhood subcortically in the brain-stem. Their function is to compound the activity of the whole body musculature to what we call "*posture.*" The lower centres for the muscles of the different parts of the body are arranged segmentally in the spinal cord; the higher centres in the brain-stem put them into combined action, and in this way govern the posture of the animal as a whole. We have here a very good example of what Sherrington has called the "integrative action of the nervous system." And integration is especially necessary in the case of posture, because nervous excitations arising from very different sense organs are flowing towards the postural centres in the brain-stem, and must be combined so that a harmonising effect will result.

Nervous impulses, which can influence posture, arise: (1) From the labyrinths, a double sense-organ: the otoliths reacting to changes in position, the ampullae of the semicircular canals to accelerations; (2) from the proprioceptive sense-organs in muscles, joints and tendons; (3) from exteroceptive nerve endings of the body surface, chiefly from the pressure sense-organs, which are stimulated, if the body touches the ground; (4) from telereceptors, reaction to distance stimuli, such as the eye, the ear, the nose. In fact a very finely elaborated central apparatus is needed to combine and distribute all these afferent impulses, depending on and adapted to the always changing circumstances of environment.

Suppose a cat is standing in the middle of the room, and a mouse is running on its right side along the wall. The optic and acoustic stimuli act on the telereceptors of the cat's head, and make it turn the heavy head to the right. By this the centre of gravity of the fore part of the body is displaced to the right. At the same time tonic neck reflexes are evoked, by which the vertebral column is curved and the right fore-limb strongly extended, so that it carries the weight of the body alone and prevents it from falling. The left fore-limb has nothing to carry, and in harmony therewith this limb relaxes under the influence of the tonic neck reflex. At the same time the distribution of excitability in the motor centres of the spinal cord is rearranged by the turning of the neck, so that, if for some reason running movements begin, the limb which has no static function will always make the first step. In this way the moving mouse impresses on the cat through the mediation of tonic neck reflexes an attitude, by which the cat is focussed towards the mouse and made ready for movement. The only thing the cat has to do is to decide: to jump or not to jump; all other things have been prepared beforehand reflexly under the influence of the mouse, which will be the object of the resulting jump.

These examples may give an impression of the different ways in which the tonic labyrinthine and neck reflexes are used during the normal life of intact animals. They can easily be extended by watching various kinds of animals. Only in the monkey they cannot easily be detected, because with the higher development of the fore-brain and the greater complication of movements these lower postural reflexes are partly suppressed. It is necessary to decerebrate or narcotise a monkey in order to show that he has the same attitudinal reflexes, obeying the same laws, as are shown by other animals.

Also, in man during ordinary life the attitudinal reflexes cannot easily be detected. In the infant child several of them are present. In adults instantaneous photographs show sometimes postures in agreement with the laws of attitudinal activity of the brain-stem centres. I owe to Dr. Wolf the acquaintance with fast cinema photos of golf players, showing that at the top of the swing the shoulders are turned by 180° in relation to the head, which is kept fixed in space as firmly as possible. In this way a tendency is evoked to extend the left arm and to twist the body to the left—movements which appear to be performed, indeed, by the subsequent photographs, and which seem to be facilitated and strengthened by the preliminary starting posture of the head and body. It is this fixing of the head in the line of sight of the ball which is insisted upon as essential to the performance of a correct shot.

CHAPTER VIII

MISCELLANEOUS

IN THIS chapter are included a group of miscellaneous passages, relating to nutrition and the endocrines. As the annotations to the individual selections explain the significance of each one, no further general statement will be included here. The passage from Claude Bernard is placed at the end because it indicates the pathway along which physiology is travelling at the moment, and along which it is likely to travel for some years to come. Out of the past sometimes come surprising divinations of the future!

CAPTAIN COOK

Captain James Cook (1728-1779) was one of the first navigators who was able to prevent outbreaks of scurvy during long sea voyages. He was a careful observer and had studied in detail the clinical symptoms of this devastating ailment. Through a series of well conducted experiments on his own men, and through comparison of his experience with that of other sea-captains, Cook concluded that certain articles of food served to keep his crew in health. Sir Joseph Banks, who had accompanied Cook on his first voyage, persuaded him, some years later, to read a paper before the Royal Society. The following extract is taken from this memorable communication[1] for which Cook was awarded the Copley Medal.

THE METHOD TAKEN FOR PRESERVING THE HEALTH OF THE CREW OF HIS MAJESTY'S SHIP THE RESOLUTION DURING HER LATE VOYAGE ROUND THE WORLD

To Sir John Pringle, Bart. P.R.S.

Mile-end,
March 5, 1776.

Sir,

R. Mar. 7, 1776.

As many gentlemen have expressed some surprise at the uncommon good state of health which the crew of the Resolution, under my command, experienced during her late voyage; I take the liberty to communicate to you the methods that were taken to obtain that end. Much was owing to the extraordinary attention given by the Admiralty, in causing such articles to be put on board, as either by experience or conjecture were judged to tend most to preserve the health of seamen. I shall not trespass upon your time in mentioning all those articles, but confine myself to such as were found the most useful.

---

[1] Cook, J. "The method taken for preserving the health of the crew of His Majesty's ship the *Resolution* during her late voyage around the world. Addressed to Sir John Pringle, Bart. P.R.S." *Phil. Trans. Roy. Soc.*, vol. 66, 1776 (pp. 402-403).

We had on board a large quantity of Malt, of which was made sweetwort, and given (not only to those men who had manifest symptoms of the scurvy, but to such also as were, from circumstances judged to be most liable to that disorder) from one to two or three pints in the day to each man, or in such proportion as the surgeon thought necessary; which sometimes amounted to three quarts in the twenty-four hours. This is without doubt one of the best anti-scorbutic sea-medicines yet found out; and if given in time will, with proper attention to other things, I am persuaded, prevent the scurvy from making any great progress for a considerable time: but I am not altogether of opinion, that it will cure it in an advanced state at sea.

Sour Krout, of which we had also a large provision, is not only a wholesome vegetable food, but, in my judgment, highly antiscorbutic, and spoils not by keeping. A pound of it was served to each man, when at sea, twice a week, or oftener when it was thought necessary.

Portable Soup or Broth, was another essential article, of which we had likewise a liberal supply. An ounce of this to each man, or such other proportion as was thought necessary, was boiled with their pease three days in the week; and when we were in places where fresh vegetables could be procured, it was boiled with them and with wheat or oatmeal, every morning for breakfast, and also with dried pease and fresh vegetables for dinner. It enabled us to make several nourishing and wholesome messes, and was the means of making the people eat a greater quantity of greens than they would have done otherwise.

CARL VON VOIT

Carl von Voit (1831-1908) of Amberg became one of the pioneers in the study of nutrition by the modern approach. He introduced many new methods of procedure for the estimation of metabolic exchange, and studied the history of each of the three cardinal foodstuffs, demonstrating among other things that fats could be formed from carbohydrates. In 1881 he published a "Handbuch" on the physiology of metabolism which served as a great stimulus to investigators in this field of work. The following extract, translated by Lusk,[2]

[2] Lusk, G. *The elements of the science of nutrition.* Philadelphia and London: W. B. Saunders Co., 844 pp., 1928 (pp. 43-45).

represents the summary of his beliefs concerning metabolism and is in reality his final pronouncement in the field which he had made so peculiarly his own.[3]

METABOLISM

The unknown causes of metabolism are found in the cells of the organism. The mass of these cells and their power to decompose materials determine the metabolism. It is absolutely proved that protein fed to the cells is the easiest of all the food-stuffs to be destroyed, next carbohydrates, and lastly fat. The metabolism continues in the cells until their power to metabolize is exhausted. All kinds of influences may act upon the cells to modify their ability to metabolize, some increasing it or others decreasing it. To the former category belong muscular work, cold of the environment (in warm-blooded animals), abundant food, and warming the cells. To the latter, cooling the cells, certain poisons, etc.

In speaking of the power of the cells to metabolize, I have not meant thereby, as may be seen from all my writings, that the cells must always use energy in order to metabolize, but rather I have understood thereby the sum of the unknown causes of the metabolic ability of the cells—as one speaks of the fermentative "power" of yeast cells.

The metabolism of the different food-stuffs varies with the quality and quantity of the food. Protein alone may burn, or little protein and much carbohydrate and fat. I have determined the amount of the metabolism of the various food-stuffs under the most varied conditions. All the phases of metabolism originate from processes in the cells. In a given condition of the cells available protein may be used exclusively if enough be furnished them. If the power of the cells to metabolize is not exhausted by the protein furnished, then carbohydrates and fats are destroyed up to the limit of the ability of the cells to do so.

From this use of materials arise physical results, such as work, heat, and electricity, which we can express in heat units. This is the power derived from metabolism.

It is possible to approach the subject in the reverse order, that is, to study the energy production (Kraftwechsel) and to draw conclusions regarding the metabolism (Stoffwechsel). It is perfectly possible to say that the requirement of energy in the body or the production of the heat necessary to cover heat loss, or for energy to do work, are controlling factors of the metabolism; since on cooling the body or on working correspondingly more matter is destroyed. But one must not conclude that the loss of body heat and muscular work are the immediate causes of this increased metabolism. The causes lie in the peculiar conditions of the organism, and muscle work and loss of heat are merely factors acting favorably upon those causes, raising the power of the cells to metabolize. In virtue of this more is destroyed, and secondarily the power to work and increased heat production are determined.

---

[3] Voit, C. von. *Münchener Med. Woch.*, Bd. 49, p. 233, 1902.

The requirement for energy cannot possibly be the cause of metabolism, any more than the requirement for gold will put it into one's pocket. Hence the production of energy has a very definite upper limit, which is afforded by the ability of the cells to metabolize. If the cells will metabolize no more, then further increase of work ceases even in the presence of direst necessity; and this is also the case with the heat production, even though it were very necessary, and we were likely to freeze.

I therefore maintain my "older" point of view, that of pure metabolism, in order to explain the phenomena of nutrition. I am convinced that it is the right way, and that the clearest and most unifying development will be possible as one investigates what substances are destroyed under different circumstances, such as the performance of work, and loss of heat, and how much of the different materials must be fed to maintain the body in condition.

FREDERICK GOWLAND HOPKINS

Sir Frederick Gowland Hopkins, Professor of Biochemistry at Cambridge, the details of whose work are described elsewhere, initiated modern investigation upon the vitamins. The following passage[4] is taken from his first paper, now one of the classics of physiological literature.

FEEDING EXPERIMENTS ILLUSTRATING THE IMPORTANCE OF ACCESSORY FACTORS IN NORMAL DIETARIES

The experiments described in this paper confirm the work of others in showing that animals cannot grow when fed upon so-called "synthetic" dietaries consisting of mixtures of pure proteins, fats, carbohydrates, and salts. But they show further that a substance or substances present in normal foodstuffs (*e.g.* milk) can, when added to the dietary in astonishingly small amount, secure the utilization for growth of the protein and energy contained in such artificial mixtures.

---

[4] Hopkins, F. G. "Feeding experiments illustrating the importance of accessory factors in normal dietaries." *Jour. Physiol.*, vol. 44, pp. 425-460. 1912. (pp. 425-426, 499-50).

The particular experiments, of which an account is now to be given, were undertaken to put upon a more quantitative basis results which I obtained as far back as 1906-07.[5] Since that time, a fuller realization of the fact that (leaving on one side the influence of the inorganic constituents of dietaries) protein supply and energy supply do not alone secure normal nutrition, has arisen from the extremely interesting recent work upon the etiology of such diseases as beri-beri and scurvy. It is not surprising that much work is now being done in connection with the subject; and since the experimental results given in this paper were obtained, the publications of others have covered part of the ground. In particular I may refer to the work of Stepp upon mice, and to the extensive researches of Osborne and Mendel upon rats. But the observations now to be described differ in some important details from those of the authors quoted. They bring out in particular the marked influence of minute additions of normal food constituents in promoting the nutritive power of synthetic dietaries. Stepp approached the subject on the lines of an attempt to estimate the importance of lipoids in nutrition. He found that food mixtures after extraction with lipoid solvents could not maintain life in mice. The total material extracted by the solvents when added to the diet made the food efficient once more; but Stepp was unable to obtain this result by adding any known lipoid. . . . .

Final discussion

Convinced of the importance of accurate diet factors by my own earlier observations, I ventured, in an address delivered in November, 1906, to make the following remarks:

"But, further, no animal can live upon a mixture of pure protein, fat, and carbohydrate, and even when the necessary inorganic material is carefully supplied the animal still cannot flourish. The animal body is adjusted to live either upon plant tissues or the tissues of other animals, and these contain countless substances other than the proteins, carbohydrates, and fats. Physiological evolution, I believe, has made some of these well-nigh as essential as are the basal constituents of diet, lecithin, for instance, has been repeatedly shown to have a marked influence upon nutrition, and this just happens to be something already familiar, and a substance that happens to have been tried. The field is almost unexplored; only is it certain that there are many minor factors in all diets, of which the body takes account. In diseases such as rickets, and particularly in scurvy, we have had for long years knowledge of a dietetic factor; but though we know how to benefit these conditions empirically, the scale errors in the diet are to this day quite obscure. They are, however, certainly of the kind which comprises these minimal qualitative factors that I am considering. Scurvy and rickets are conditions so severe that they force themselves upon our attention; but many other nutritive errors affect the health of individuals to a degree most important to themselves, and some of them depend upon unsuspected dietic factors."

---

[5] The results of experiments made at this time were summarized in Lectures delivered at Guy's Hospital in June, 1909. Owing to subsequent ill health these Lectures were never published. The results given in the present paper were communicated to the Biochemical Club in October, 1911. See also *Analyst,* xxxi, p. 395, 1906.

Evidence has now accumulated from various sides to justify these views. That a deficiency in quite other factors can induce disease is a fact which is now upon a firm experimental basis. That a deficiency, quite as little related to energy supply, may result in the failure of so fundamental a phenomenon as growth in young animals seems equally certain. To what extent bare maintenance of the body-weight is possible, in spite of such deficiencies, is perhaps less certain. Osborne and Mendel observed prolonged maintenance on artificial mixtures, but found that "sooner or later the animals declined; and, unless a change in the diet was now instituted, within a comparatively short period the animals died." I have myself seen quite young rats maintain their weight practically unaltered upon a casein mixture for three weeks, and then begin to lose weight, or on the other hand, if given the necessary small addendum, begin to grow briskly. Such observations give the impression that the factor missing from the artificial food is one concerned solely with growth. But it is certain, as Stepp also found, that the presence of a most extraordinarily small remainder of the substance or substances removable by alcohol extraction, can affect the physiological value of artificial diets; and I am inclined to believe that apparent maintenance (which is usually very slow growth, or very slow decline) is only seen when the diet is not wholly free from them. If the food has been very thoroughly extracted, and if the fat subsequently added is wholly free from any tissue elements, I venture to think that only very short maintenance is possible. That "Denaturierung" plays no part here is shown by the fact that such food is clearly utilised when associated with a small addendum of the kind being discussed.

CASIMIR FUNK

Casimir Funk, formerly of the Department of Biochemistry in the School of Hygiene at Warsaw, is well known to physiologists for his pioneer contribution in the field of the vitamins. In a paper of seven pages he established the fact that beri-beri is due to the lack of a specific chemical substance in rice polishings, and that a dose of the active extract containing only 4 mgr. of nitrogen promptly relieved symptoms of polyneuritis in pigeons. Funk received his Ph.D. from the University of Berne in 1904 and his D.Sc. in 1913 in London after several years work at the biochemical department of the Lister Institute, where he carried out his investigations on vitamins. The following selections are taken from his first paper.[6] In a second paper, 1912, which also appeared in the *Journal of Physiology,* he introduced the term "vitamine" in the false belief that all accessory food factors were "amine" derivatives.

BERI-BERI AND RICE POLISHINGS

As a result of the work of a number of observers (Eykman,[7] Gryns,[8] and Stanton[9]) it has been shown that the cortical layers of rice contain a substance which cures beri-beri in man and the polyneuritis which is produced in birds by feeding them on polished rice.

The present inquiry is directed to determine the chemical nature of the curative substance.

The experiments were carried out on pigeons of which a large stock was kept. Polyneuritis was induced by feeding on ordinary polished rice. The average time before the onset of symptoms was three weeks. The presence or absence of the active principle in the different fractions, obtained during the investigation of rice-polishings, was determined by administering them to pigeons already severely affected with polyneuritis and observing the result. The condition of the birds at the time of the tests was such that untreated they succumbed within 12 hours.

May it be here mentioned that the extracts, if given in too large a dose, were poisonous. This, as will be shown later, was due to the presence of choline which accompanied the active principle until the final stage of the separation. The poisonous action can be avoided by giving a dose calculated on the quantity of polishings used. With suitable doses passed into the crop by a tube, the pigeons recovered in 6-12 hours. Often, even after three hours the bird seemed quite well.

---

[6] Funk, C. "On the chemical nature of the substance which cures polyneuritis in birds induced by a diet of polished rice." *Jour. Physiol.,* vol. 43, pp. 395-400, 1911 (pp. 395, 400).

[7] Eykman. Virchow's Arch. 148, 523, 1892; *Ibid.,* 149, 187, 1897. Arch. f. Hygiene, LVIII, 150 (1906).

[8] Gryns quoted by Schaumann. Arch. f. Schiffs-und Tropenhygiene, 1910.

[9] Fraser and Stanton. Studies from the Institute for Medical Research. Federated Malay States. No. 12. The etiology of beri-beri, 1911.

One symptom of polyneuritis in pigeons is paralysis of the crop and the birds being also generally paralysed the dose administered is very likely to run out again unless the head is supported. A further possible source of error occurs when the crop is not completely paralysed as the bird can vomit the material.

Although the active substance has been definitely identified with the Ag salt obtained by precipitating with $AgNO_3$ in presence of baryta, the proof of activity of the nitrate obtained from this Ag salt and which was the salt submitted to analysis is less conclusive, as by this time the exhaustion of the material permitted of but four experiments, three of which were successful and one failed to cure the bird. For the same reason it was not possible to investigate further the chemical reaction of the substance but attempts to obtain by extraction of more raw material the active substance from other food-stuffs are in progress.

SUMMARY

Polyneuritis of birds as shown by Eykman, Gryns, Fraser and Stanton, is due to the lack of an essential substance in the diet. The substance is only present in minute amount, probably not more than 1 grm. per kilo of rice.

The substance which is absent in polished rice and is contained in rice-polishings is an organic base which is completely precipitated by phosphotungstic acid and by silver nitrate and baryta. It is partially precipitated by mercury chloride in alcoholic solution in the presence of choline and is not precipitated by platinum chloride in alcoholic solution.

Reasons for provisionally regarding the active substance as a body giving a crystalline nitrate which has the percentage composition of 55.63%C, 5.29%H and 7.68%N are adduced, but as by the time the search had approached the final stages the material became exhausted; duplicate analyses could not be made and but few animal experiments performed.

The chemical nature of the curative substance could not be further investigated immediately but larger quantities of raw material are being worked up.

The curative does of the active substance is small; a quantity of substance which contains 4 mgr. of nitrogen cured pigeons.

GEORGE OLIVER AND EDWARD SHARPEY SCHAFER

G. Oliver and Sir Edward Sharpey Schafer were the first to isolate the active principle of a ductless gland and to investigate its physiological effects. It is difficult to realize that the enormous growth of knowledge concerning the endocrines has taken place almost entirely since 1894, when Oliver and Schafer discovered the potency of an extract of the suprarenals. The thyroid was soon studied, and cretinism had proved curable by feeding of the whole gland. Then came pituitrin, and, after an interval, insulin and parathormone. The extract of the glands of reproduction is still under investigation, but there is every reason to believe that the active principles will soon be known. The following passage on the isolation of adrenal secretion is taken from the original announcement of Oliver and Shafer.[10]

ON THE PHYSIOLOGICAL ACTION OF EXTRACT OF THE SUPRARENAL CAPSULES

The suprarenal capsules yield to water (cold or hot), to alcohol or to glycerine a substance which exerts a most powerful action upon the blood vessels, upon the heart, and upon the skeletal muscles. These effects have been investigated upon the dog, cat, rabbit and frog. In the frog the solutions were injected into the dorsal lymph-sac, in the rabbit subcutaneously and into a vein, in the other animals into a vein. The alcohol extracts were first dried and the residue extracted with normal saline; the watery decoctions were made with normal saline, and the glycerine extracts were largely diluted with the same previous to injection. The doses employed have varied from a mere trace up to an amount of extract equivalent to 3 grains (0.2 gramme) of the fresh gland; in one or two instances we have given larger doses with the object of obtaining if possible a lethal result. The extracts used have been made from the suprarenals of the calf, sheep and dog. Exactly similar effects have been obtained in each case. Except in the case of the frog we have not obtained any marked effect from subcutaneous injections of comparatively small doses. . . . .

The effect upon the blood vessels is to cause extreme contraction of the arteries, so that the blood-pressure is enormously raised. This is most evident when the vagi are cut in order to obviate the inhibitory action upon the heart which otherwise occurs; it is also seen after section of the cervical cord. The blood-pressure may rise from 2 to 4 times above normal. This extreme contraction of the vessels is evidenced by the plethysmograph; section of the nerves going to the limb produces no difference in the result. The effect is therefore peripheral. This can also be shown in the frog with its nerve-centres destroyed, and through the blood vessels of which normal saline is allowed to circulate; if only a small quantity of suprarenal extract is added to the saline the flow almost entirely ceases.

---

[10] Oliver, G. and E. A. Schafer. "On the physiological action of extract of the suprarenal capsules." *Jour. Physiol.* (Proc.), vol. 16, pp. i-iv, 1894 (pp. i-iii).

The time which elapses between the injection into a vein and the first effect upon the blood vessels is in the dog from 25 to 30 seconds. But if an experiment has been conducted for some three hours or more, the animal during the whole of this time having been under the influence of morphia and curare, the contraction of the vessels of a limb is preceded by a preliminary expansion, the cause of which is as yet not clear. It is however a constant phenomenon. . . . .

The effect upon the skeletal muscles has been investigated in the frog. The movements of a frog to which a hypodermic injection of extract of suprarenal capsule (equal to 1 or 2 grains of the fresh gland) have been given soon become slow, and after about half-an-hour the reflexes are very faint and almost abolished; the animal soon appears completely paralysed. The muscles however still contract on being stimulated, either directly or through the motor nerves, but the contractions are modified, the relaxation period being greatly prolonged, as with veratria poisoning. The period of latent stimulation is not greatly, if at all, lengthened. The fatigue curves were rapidly developed. The effect is not at all comparable to that produced by curare.

We have noticed a slight effect to be produced upon the respiration, which may become shallower; but in the doses we have used the result was very slight when compared with the prodigious effects upon the heart and blood vessels which were obtained.

FREDERICK GRANT BANTING, CHARLES HERBERT BEST AND JOHN JAMES RICKARD MACLEOD

Frederick Grant Banting, Charles Herbert Best, and John James Rickard Macleod gave the first description in print of the successful isolation of insulin.[11] The story of Banting's original idea and of his subsequent collaboration with Best and Collip has been delightfully told by Macleod,[12] in whose laboratory the experiments were performed, and need not be repeated here. The first successful experiment was carried out on August 10, 1921, and within less than a year insulin was available in every corner of the world for the treatment of diabetes. The following passage is the full text of the original announcement of the discovery. The next paper, in which further details were given, was by Banting and Best and appeared early in 1922 in the *Journal of Laboratory and Clinical Medicine.*

---

[11] Banting, F. G., Best, C. H. and Macleod, J. J. R. "The internal secretion of

THE INTERNAL SECRETION OF THE PANCREAS

The hypothesis underlying our experiments was that the usual extracts of pancreas do not satisfactorily demonstrate the presence of an internal secretion acting on carbohydrate metabolism, because this is destroyed by the digestive enzymes also present in such extracts. To circumvent this difficulty we have taken advantage of the fact that the acinous, but not the insular cells become degenerated in seven to ten weeks after ligation of the ducts.

A neutral or faintly acid extract of the degenerated gland, kept at a low temperature, was therefore prepared and its effect on pancreatic diabetes investigated. Ten weeks after ligation of the pancreatic ducts the degenerated gland was removed and extracted with ice-cold Ringer's solution. This extract injected intravenously or subcutaneously invariably caused marked reduction of the percentage of sugar in the blood and the amount of sugar excreted in the urine. Extracts of liver, spleen or boiled extract of degenerated pancreas have no effect.

Further investigations have shown the following: *a,* incubation of the extract, in alkaline reaction, for 2 hours, with pancreatic juice removes its effect; *b,* glucose given intravenously or per os is retained by diabetic animals if adequate doses of the extract are also administered; *c,* the clinical condition of the animal is improved by the extract; *d,* hemoglobin estimations before and after administration of the extract are identical; *e,* neutral extract kept in cold storage retains its potency for at least seven days; *f,* subcutaneous injections have a less rapid but more prolonged effect. Rectal injections are not effective.

The experiments have been repeated on ten animals several of which were under observation for over 2 weeks.

---

the pancreas." Proc. Amer. Physiol. Soc., New Haven, Dec. 28, 1921. *Amer. Jour. Physiol.,* vol. 59, p. 479, 1922.

[12] Macleod, J. J. R. *Carbohydrate metabolism and insulin.* London: Longmans, xii+357 pp., 1926.

CLAUDE BERNARD

Claude Bernard (1813-1878), one of the greatest names in the history of physiology, has left his mark on so many branches of the subject that it is impossible to say which of his many discoveries was the most significant:- vasomotor nerves, glycogen and carbohydrate metabolism, curare and muscle; perhaps greater than all these was his teaching concerning the internal environment of the organism, Bernard's last published work, and the outcome of a life of profound thought. Little appreciated at the time, this far-reaching conception has now come into its own,[13] and as it will undoubtedly exert a great influence on the physiology of the future, I have selected as the closing passage of this book Bernard's simple description of the *milieu intérieur.*[14]

THE MILIEU INTÉRIEUR

The various ways in which living organisms are related to their cosmic environment enable us to study life in three forms according as existence is entirely dependent upon external conditions, less dependent, or relatively independent. These three forms of life are as follows:

1. *Vie latente,* where life is not evident.
2. *Vie oscillante,* where evidences of life are variable and dependent upon external environment (milieu extérieur).
3. *Vie constante,* where life manifests itself independently of the external environment.

* * * * * *

III. The third form of existence, characterised by freedom and independence is found in the more highly organised animals. Here life is never suspended, but flows steadily on apparently indifferent to alterations in its cosmic environment or changes in its material surroundings. Organs, structural mechanisms and tissues all function uniformly and their operations show no sign of the considerable variations present in organisms where conditions are inconstant. This is due to the fact that the *milieu intérieur* surrounding the organs, the tissues and their elements never varies; atmospheric changes cannot penetrate beyond it and it is therefore true to say that the physical conditions of environment are unchanging in a higher animal: each one is surrounded by this invariable *milieu* which is, as it were, an atmosphere proper to itself in an ever-changing cosmic environment. Here we have an organism which has enclosed itself in a kind of hot-house. The perpetual changes of external conditions cannot reach it; it is not subject to them, but is free and independent.

---

[13] "Stability may sometimes be afforded by the natural environment, as in sea water. In other cases an integument may sufficiently temper the external changes. But by far the most interesting protection is afforded, as in man and higher animals, by the circulating liquids of the organism, the blood plasma and lymph, or, as Claude Bernard called them, the *milieu intérieur.* In his opinion, which I see no reason to dispute, the existence and the constancy of the physico-chemical properties of these fluids is a necessary condition for the evolution of free and independent life. This theory of the constancy of the *milieu intérieur* was an induction from relatively few facts, but the discoveries of the last fifty years and the introduction of physico-chemical methods into physiology have proved that it is well founded." (Henderson, L. J. *Blood. A study in general physiology,* New Haven: Yale Press, 1928, p. 20).

[14] Bernard, C. *Leçons sur les phénomènes de la vie commmuns aux animaux et aux vegetaux.* Paris: Ballière, 1878, 2 tomes, xxxii+564 pp. (tom. 1, pp. 67, 111-114, 123-124).

I think I was the first to urge the belief that animals have really two environments: a *milieu extérieur* in which the organism is situated, and a *milieu intérieur* in which the tissue elements live. The living organism does not really exist in the *milieu extérieur* (the atmosphere if it breathes, salt or fresh water if that is its element) but in the liquid *milieu intérieur* formed by the circulating organic liquid which surrounds and bathes all the tissue elements; this is the lymph or plasma, the liquid part of the blood which, in the higher animals, is diffused through the tissues and forms the ensemble of the intercellular liquids and is the basis of all local nutrition and the common factor of all elementary exchanges. A complex organism should be looked upon as an assemblage of simple organisms which are the anatomical elements that live in the liquid *milieu intérieur.*

The stability of the *milieu intérieur* is the primary condition for freedom and independence of existence; the mechanism which allows of this is that which ensures in the *milieu intérieur* the maintenance of all the conditions necessary to the life of the elements. From this we know that there can be no freedom or independence of existence for simple organisms whose constituent parts are in direct contact with their cosmic environment, and that this form of life is, in fact, the exclusive possession of organisms which have attained the highest state of complexity or organic differentiation.

Stability of environment implies an organism so perfect that it can continually compensate for and counterbalance external variations. Consequently, far from the higher animals being indifferent to their surroundings, they are on the contrary in close and intimate relation to it, so that their equilibrium is the result of compensation established as continually and as exactly as if by a very sensitive balance.

The necessary conditions for the life of the elements which must be brought together and kept up constantly in the *milieu intérieur* if freedom and independence of existence are to be maintained are already known to us: water, oxygen, heat, and reserve chemical substances.

These are the same conditions as are necessary for life in simple organisms; but in the perfected animal, whose existence is independent, the nervous system is called upon to regulate the harmony which exists between all these conditions.

★ ★ ★

Conclusion. We have examined in turn the three general forms in which life is evident: *vie latente, vie oscillante, vie constante,* in order to see if in one of them we could find a vital internal principle capable of causing manifestations of life independently of external physico-chemical conditions. The result of our search is easily seen. We have found that in a state of latent existence the organism is dominated by external physico-chemical conditions to such a degree that all evidences of life can be stopped. In the variable state (*vie oscillante*) though the living organism is not entirely subordinate to external conditions, yet it is so bound up in them that it is subject to all their variations. In the constant state of existence (*vie constante*) the living organism appears to be free and its manifestations of life seem to be produced and regulated by an internal vital principle, free from the restraint of external physico-chemical conditions; this appearance is an illusion. On the contrary it is in the mechanism of an existence characterised by freedom and independence that the close relationship between the organism and external conditions is particularly evident.

We cannot therefore admit, in living organisms, a free vital principle which fights against the influence of physical conditions. The opposite has been proved and thus it overthrows all the contrary conceptions of the vitalists.

INDEX OF AUTHORS, SUBJECTS, AND BOOK-TITLES

Chief references are indicated in heavy type.

- Abernethy, J., 250.
- *Absorbing vessels of human body* (Cruikshank) 159.
- Acapnia, 130, 131, 132.
- Accessory factors, 299.
- Action currents, discovery of, 209.
  - muscle, 209.
  - nerve, 229.
  - reflexes, 220.
- Adaptation, nerve, 232.
- Adrenaline, discovery of, 299.
- Adrian, E. D., 220, **232.**
- Aikin, J., 119.
- Air, composition of, 122.
  - weight of, 7.
- Aldini, G., 210.
- All-or-none principle, 181, 214, 221.
- *L'âme raisonnable,* 236.
- Anastomoses and valves, 41.
- *Anatomicarum institutionum* (Guenther) 44.
- Animal electricity, 209.
- *Annalen* (Poggendorff) 18.
- Anoxæmia, 132.
- Apnœa, 128, 131, 132.
- Aristotle, 37, **38,** 106, 181.
  - *De partibus animalium,* 38.
- Arnold, 137.
- Arrhenius, S., viii, 3, **23,** 25.
- Artificial respiration, 109.
- Aselli, G., 144 (portr:), **145,** 159, 160, 161.
- Asellius, see Aselli.
- Asphyxiation and shock, 130.
- Attitudinal reflexes, 294.
- Autoxidation, 135.
- Avogrado, 25.

- Ballance, C., 282.
- Banks, J., 12, 15, 296.
- Banting, F. G., **305,** 306.
- Barcroft, J., ix, 107, **131.**
- Barnard, C., 44.
- Bartholin, T., 160, 161.
- Bayliss, W. M. **26,** 27 (portr:), 140.
- Beaumont, W., ix, 139, **164,** 166 (portr:), 167.
  - *Observations on the gastric juice,* 167.
- Beddoes, T., 112.
- Bell, C., 235, 250, **251,** 252, 264, 265.
  - *New anatomy of the brain,* 252.
- Beri-beri, cause of, 302.
- Bernard, C., 94, 218, 279, 280, 281, 296, **307.**
  - *Phénomènes de la vie,* 307.
- Bert, P., 132.
- Best, C. H., **305,** 306.
- *Bibliotheca Osleriana,* ix.
- Black, J., 61, 82, **91,** 93.
- Blagden, C., viii, ix, **11,** 12, 15.
- *Blood* (Henderson), 34, 307.
- Blood, transfusion of, 116.
- Blood vessels, see capillaries.
- Borelli, G. A., 62, 192, **202.**
- Bowditch, H. P., 174, **213,** 216 (portr:).
- Boyle, R., ix, 3, **6,** 23, 24, 106, **107,** 109, 111, 112, 152, 192.
  - *Sceptical Chymest,* 6, *Spring and Weight of the air,* 6, 107. *Continuation of new experiments,* 107.
- Boyle's Law, dilute solutions and, 23.
  - original descriptions of, 7.
- Brown, R., **15.**
- Browne, J., 38.
- Brownian movement, 16.
- Brown-Séquard, C. E., **278,** 280.
- Brown-Séquard paralysis, 280.
- Brücke, E. W., 221, 232.
- Burke, E., 120.

- Cæsalpinus, A., 6.
- Calcination, 4, 123.
- Calvin, J., 43, 44.
- Canano, G., 47.
- Cannon, W. B., viii, 139, **174.**
- Capillaries, Ch. III, 61, *et seq.*
  - contractility of, 86, 98.
  - effects of substances perfused, 87.
  - increase during activity, 100.
  - shifting of, 102.
  - white reaction and, 103.
- *Capillary circulation* (Black) 91.
- *Capillary circulation of bactrachia* (Hall) 91.
- Carbon dioxide and shock, 130.
- Carbon monoxide poisoning, 130.
- Cardan, J., 6.
- Cathode ray oscillograph, 229.
- Central nervous system, see nervous system.
- Cerebellum, Walker on, 251.
  - Flourens on, 268.
- Charcot, J. M., 282.
- *Christianismi restitutio* (Servetus) 44.
- Chronaxie, 218.

Cigna, 124.
Circulation of the blood, 37, 52, 57.
Clark-Kennedy, A. E., 75.
Clonus, 288.
Collip, J. B., 306.
Combustion, respiration and, 107.
Conservation of energy, 18.
Continuation of new experiments (Boyle) 107.
Contraction, see muscle.
'Contraction with metals', 209.
Cook, J., **296.**
Costaeus, J., 146.
Croone, W., 181, **185,** 292.
Cruikshank, W. C., 158 (portr:), **159.**
Curare, 218.
Cushing, H., ix, **289.**

Dale, H. H., 100.
De corde (Lower) 116.
Decrementless conduction (Kato) 225.
Decrementless conduction, 226.
De Graaf, R., vii, viii, 139, 146, **147** (portr:), 149.
  De usu succi pancreatici, 146.
De homine (Descartes) 236.
De lactibus (Aselli) 145.
De motu animalium (Borelli) 192.
De motu cordis (Harvey) 51.
De motu musculorum (Galen) 182.
Denys, 116.
De partibus animalium (Aristotle) 38.
Dephlogisticated air, Lavoiser on, 125.
  Priestley on, 120.
De pulmonibus (Malpighi) 37.
De rachitide (Mayow) 113.
De ratione motus musculorum (Croone) 185.
De respiratione (Mayow) 112-113.
De Rey-Pailhade, 135, 137.
Descartes, R., 207, 235, **236,** 245.
  De homine, 236.
De structura et motu musculare (Stuart) 206.
De trinitatis erroribus (Servetus) 44.
De usu partium (Galen) 41.
De usu succi pancreatici (de Graaf) 146.
De venarum ostiolis (Fabricius) 47.
De ventriculo et intestinis (Glisson) 199, 200.
De viribus electricitatis (Galvani) 209.
Digestion, Ch. V., 139 *et seq.* See gastric juice.
  gastric juice and, 140, 146, 149.
  insensible perspiration and, 140.
  stomach movement and, 176.
  stomach pouch, 170.
Digestive glands (Pavlov) 170.
Dilute solutions, 23.
Dipeptide, 136.
Dissociation, 25.
Doorlets of veins, see valves.
Douglas, G., 133, 134.
Du Bois-Reymond, 18.
Duval, M., 94.

Ebbecke, U., 103.
Einstein, A., 16, 17.
Elemental Physiologiæ (Haller) 82, 86.
Elements of science of nutrition (Lusk) 297.
Endocrines, 296.
Energy, conservation of, 18.
Environment, fitness of, 34.
  internal, 307.
Erhaltung der Kraft (Helmholtz) 18, 19.
Erlanger, J., **229.**
Excitability, 218.
Experiments and observations (Priestley) 120.
Eye muscles, reciprocal innervation of, 240.
Exteroceptors, 287.
Eykman, 302, 303.

Fabricius, H., viii, ix, **47,** 50, 52, 106.
  De venarum ostiolis, 47.
Fachsius, 6.
Fallopius, G., 47.
Ferriar, J., 119.
Ferrier, D., 235, **281,** 282.
Final common path, 285.
Fisica animale (Spallanzani) 155.
Fistula, pancreatic, 149.
Fitness of environment (Henderson) 34.
Fletcher, W. M., 135, **214.**
Flourens, M. J. P., 107, 235, **266.**
Fonctions du système nerveux (Flourens) 266.
Forbes, A., 220.
Fordyce, G., 12.
Foster, M., x, 62, 122, 140, 145, 206.
Franklin, K. J., 47.
Fraser, 303.
Fredericq, L., 129.
Fritsch, 235, 281.
Functions of the brain (Ferrier) 282.
Funk, C., 302.

Galen, on circulation, 37, 38, **41,** 42, 46, 106, 160.
  on muscles, **181,** 182, 203, 207.
  De usu partium, 41, *De motu musculorum,* 182.

Galvani, A. L., **209,** 210.
Gas laws, 23.
Gassendus, 107.
Gasser, H. S., **229.**
Gastric juice, Beaumont on, 167.
  Cannon on, 174.
  Pavlov on, 170.
  Réamur on, 152.
  Spallanzani on, 155.
Gay-Lussac, J. L., 20.
Geppert, 129.
Gibbs, J. W., 18, 34.
Glisson, F., 161, 181, 198 (portr:), **199.**
Glutathione, 135.
Godeheu, 154.
Goltz, F. L., 281.
Gotch, F., 220.
Gregg, A., 220.
Gryns, 302, 303.
Guenther, J., 43.

Hahn, L., 94.
Haldane, J. S., ix, **31,** 33, 107, **126.**
  Respiration, 32.
Hales, S., **57,** 61, **75,** 124, 235.
  Statical essays, 75.
Hall, M., 91, 129, 235, 270 (portr:), **271,** 272.
  Capillary circulation of batrachia, 91.
Haller, A., von, viii, **82,** 83 (portr:), 86, 91, 160, 162, 181, 274.
  Elementa Physiologiæ, 82, 86.
Handbuch der Physiologie (Müller) 86.
Hartree, W., **223.**
Harvey, W., 38, **50,** 51, 57, 61, 62, 75, 79, 160.
  Prelectiones anatomiæ universalis, 51, *De motu cordis,* 51.
Hastings, C., 87, 88.
Head, F. H., 231.
Heat production, muscle, 223.
Heffter, 136, 137.
Heidenhain, R. P. H., 170.
Helmholtz, Anna von, 18.
Helmholtz, H. von, frontispiece (portr:), vii, viii, x, 3, **18,** 181.
  Erhaltung der Kraft, 18, 19.
Helmont, J. B. *van,* 139.
Henderson, L. J., **33,** 34.
Henderson, Y., **130.**
Henry, T., 119, 122.
Hewson, W., 159.
Hill, A. V., **223.**
Hippocrates, 160.
Hitzig, E., 235, 281.
Hoff, J. H., van't, 3, **22,** 23, 25.
Hooke, R., 106, **109,** 111, 117, 186.
Hopkins, F. G., **135, 214, 299.**
Hunter, J., 159, 161, 162.
Hunter, W., 159.
Huxley, T. H., 32.
Hydrochloric acid, discovery of in stomach, 163.
Hydrogen-ion concentration of blood, 132.
  acapnia and, 132, 133, 134, 135.
  anoxæmia and, 132, 133, 134, 135.
  carbon dioxide and, 133, 134, 135.
  mountain sickness and, 132, 133, 134, 135.
Hyperpnœa, 129.

Inflammation, 89.
Inhibition, vagus, discovery of, 276.
Insensible perspiration, 140.
Insulin, discovery of, 305.
Integrative action of nervous system (Sherrington) 284.
Intercostal muscles, 115.
"Internal environment," 307.
Internal secretion, see endocrines.
Interoceptors, 287.
Involuntary motions (Whytt) 242.

Jackson, H., 236.
Jolyffe, 160, 161.
Jurin, J., 80.

Kaltenbrunner, 87.
Kato, G., **225.**
Kendrew, 104.
Keynes, G. L., 51.
Khizhin, 170.
Knee jerk, 288.
Koch, R., 87.
Körperstellung (Magnus) 292.
Krogh, S. A. S., 61, 94, **100.**

Labyrinthine reflex, 294.
Lacteals, discovery of, 145.
  human, 159.
Lactic acid and muscle, 217.
Lagrange, J. L., 122.
Langley, J. N., 230.
Lapique, L., 94, **218,** 219.
Lavoisier, A. L., viii, 106, 112, 120, **122.**
Laws of vital functions (Philip) 88.
Leake, C., 51.
Leeuwenhoek, A. van, 61, **68,** 69 (portr:), 80, 81, 192.
Legallois, J. J. C., 107.
Lembert, F. J., 174.
Lepage, 179, 180.

Lewenhoeck, Lewenhook, see Leeuwenhoek.
Lewis, T., ix, 61, 100, **103**.
Libavius, A., 6.
Liddell, E. G. T., 284.
Localization, cerebral, 281.
Lovell, J., 167.
Lower, R., 79, 106, 111, **116,** 192.
Lucas, R., 218, 220.
Ludwig, C., 170, 214.
Lung, circulation in, **61,** 111, 117.
  see Respiration.
Lusk, G., 297.
Lymphatic vessels, 161.

Mackall, L. L., ix, 44.
MacLeod, J. J. R., **305,** 306.
Magendie, F., 235, 250, 252, **258,** 260 (portr:), 265.
Magnus, R., 292.
Maki, 226, 227.
Malpighi, M., ix, 37, 57, **61,** 62, 106, 114, 162, 209, 274.
  De pulmonibus, 37.
Manchester Philosophical Society, 119.
Mariotte, E., 20.
Martine, G., 80.
Mascagni, P., 162.
Massari, B., 61.
Mayer, R., 18.
Mayo, H., ix, 235, **265,** 266.
Mayow, J., viii, 106, **111,** 112, 122.
  Tractatus duo, 111.
Medicina statica (Sanctorius) 140.
Memphitic air, 126.
Mendel, 300, 301.
Metabolism, 298.
Micrographia (Hooke) 109.
Milieu intérieur, 307.
Moebius, G. M., 107.
Molecular reality, 16.
Mosso, A., 132.
Motor cortex, 281, 285, 289.
Mountain sickness, 132.
Muirhead, A. M., x.
Müller, J., vii, 18, 61, **86, 274.**
  Handbuch der Physiologie, 86, *Phantastischen Gesichtserscheinungen,* 274, *Physiologie das Gesichtssinnes,* 274.
Muscle, Ch. VI, 181 *et seq.*
  action currents of, 210, 220.
  all-or-none principle, 181, 214, 221.
  'animal electricity' and, 209.
  'animal spirits' and, 181, 189, 196, 199, 203, 207.
  Borelli on, 203.
  Croone on, 186.
  Fletcher on, 214.
  Galen on, 182.
  Glisson, on, 199.
  Hartree on, 223.
  heart, stimulation of, 214.
  heat-production of, 223.
  Hill on, 223.
  Hopkins on, 214.
  structure of (Croone), 186.
  Stuart on, 206.
  survival respiration of, 214.
  volume of, during contraction, 199.
  Willis on, 195.
Myotatic reflex, 288.

Narcotization, nerve, 226.
Nerve, Ch. VI, 181 *et seq.*
  action currents of, 230.
  adaptation and, 232.
  chronaxie of, 218.
  decrementless conduction of, 226.
  excitation of, 218.
  frequency of discharge, 221, 234.
  narcosis, 226.
  refractory period of, 233.
  rheobase of, 219.
Nerves, phrenic, 229.
  saphenous, 230.
  sciatic, 229.
Nervous system, Ch. VII, 235 *et seq.* (see also Reflexes)
  adaptation in, 232.
  anatomy of, 252.
  anterior nerve roots, 250, 255, **261**.
  Bell on, 251.
  Brown-Séquard on, 27.
  cerebellum and 251, 267, **268**.
  Cushing on, 289.
  exteroceptors of, 286.
  Ferrier on, 282.
  final common path, 285.
  Flourens on, 266.
  integration and, 284.
  Magendie on, 258.
  Magnus on, 292.
  Marshall Hall on, 271.
  Mayo on, 265.
  motor cortex and, 282, 289.
  Müller on, 274.
  Prochaska on, 247.
  posterior nerve roots, 250, 255, **261,** 262.
  proprioceptors of, 286.
  'rational soul', 236.
  receptors of, 286.
  reciprocal innervation of, 240.
  sensation and, 247, 254, 262, 271, 286, 290.

  Sherrington on, 284.
  specific 'nerve energies', 254, 274.
  'vital' motions, 245.
  Weber, E. H., and E. F., on, 276.
Newton, I., 18.

Observations on the gastric juice (Beaumont) 167.
Oesterreicher, S., 88.
Oldenburg, H., 112.
Oliver, G., viii, **304.**
Orthopnœa, 116.
Osborne, T. B., 300, 301.
Order of nature (Henderson) 33.
Osler, W., vii, ix.
Osmotic pressure, gas laws and, 23.
  of serum proteins, 29.
Oxidation, cellular, 35.
Oxidation, history of, see calcination.
Oxygen, discovery of, 123.
  Mayow on, 111.
  Priestley, 119.
  Rey on, 4.
Oxygen-want, 130, 133.

Pancreas, insulin and, 306.
  de Graaf on, 146.
Pancreatic juice, discovery of (de Graaf) 146.
  Bayliss and Starling on, 178.
  secretin and, 178.
Paschall, 10.
Pavlov, I. P., 139, **170.**
Pecquet, J., 107, 145.
Penn, W., 18.
Percival, T., 119.
Perrin, J., 15, **16.**
Perspiration, insensible, 140.
Pfeffer, A. J., 23.
Phantastischen Gesichtserscheinungen (Müller) 274.
Phénomènes de la vie (Bernard) 307.
Phipps, J., 12.
Physiological essays (Whytt) 79.
Physiologie das Gesichtsinnes (Müller) 274.
Physiology of capillaries (Krogh) 100.
Pollen, Brownian movement and, 15.
Posterior roots, Bell on, 255.
  Magendie on, 261.
Pratt, F. H., 221.
Prelectiones anatomiæ universalis (Harvey) 51.
Phlogiston, 119.
Postural reflex, 293.
Priestley, Joseph, 106, **119,** 120, 122.
Priestley, J. G., ix, 107, 124, **126.**
Prochaska, G., 235, 247.
Proprioceptive system, 286.
Proteins, osmotic pressure of, 29.
Prout, W., 139, **163,** 167.
Pulmonary circulation, 45.

Quincy, J., 140.

Rational soul, Descartes, 236.
Readings in pathology (Long) vii.
Réaumur, R. A. F. de, ix, 139, **152,** 155.
Reciprocal innervation, 240.
Reflections upon learning (Wotton) 44.
Reflexes,
  attitudinal, 294.
  Descartes and, 238.
  discovery of (Whytt), 245.
  labyrinthine, 294.
  Marshall Hall on, 271.
  Mayo on, 265.
  myotatic, 288.
  postural, 293.
  righting, 293.
  sensorium commune and, 247.
  Sherrington on, 288.
  standing, 293.
Rey, J., **4.**
Respiration, Ch. IV, 106, *et seq.*
  accessory muscles of, 114.
  air pump and, 107, 109.
  Barcroft on, 131.
  Boyle on, 107.
  colour of blood and, 117, 118.
  excess of carbon dioxide and, 126.
  glutathione and, 135.
  Henderson on, 130.
  Hooke on, 109.
  Hopkins on, 135.
  insensible transpiration and, 108.
  intercostal muscles and, 114.
  Lavoisier on, 122.
  Lower on, 116.
  Lungs and, 110, 112, 124.
  Mayow on, 111.
  memphitic air and, 126.
  necessity of air for, 107.
  orthopnœa, 116.
  Oxygen-want and, 130, 133.
  shock, loss of carbon dioxide and, 130.
  "spiritus nitro-æreus', 111.
  tissue, 135.
Respiratory centre
  Haldane and Priestley on, 128.
  Legallois, 107.
Respiration (Haldane) 32.

Rheobase, 219.
Richards, J. M., 101, 102.
Rickets, Mayow on, 111, 113.
Righting reflex, 293.
Ringer, S., 224.
Riolan, J., 52.
Rolando, L., 235, 283.
Röntgen rays, 174.
Roots, posterior,
  Bell on, 251.
  Magendie on, 258.
  Walker on, 247.
Rouget, C. M. B., 82, **94,** 95 (portr:).
Rouget cells, 94.
Rudbeck, O., 160, 161.

St. Martin, A., 139, 164, 166, 167, 168.
Sanctorius, S., ix, 139, **140.**
Scaliger, J., 6.
Sceptical chymest (Boyle) 6.
Schafer, E. S., viii, **304.**
Scheel, P., 116.
Scheele, C. [or K.] 122.
Schwann, T., 139, 167.
Scurvy, Cook on, 296.
  Hopkins on, 301.
Secretin, discovery of, 178.
Selenka, 100.
Sensation, Marshall Hall on, 271.
  Müller on, 274.
Sensorium commune, 247.
Septalius, 146.
Serum Proteins, 29.
Servetus, M., 38, **43.**
  De trinitatis erroribus, 44, *Christianismi restitutio,* 44.
Servetus and Calvin (Willis) 44.
Sharpey-Schafer, see Schafer.
Shaw, 264, 265.
Sherrington, C. S., 236, 281, **284,** 289, 292, 293.
  Integrative action of nervous system, 284.
Shock, carbon dioxide and, 130.
Singer, C., 51.
Skin, circulation in, 102, 104.
Solander, D. C., 12, 13.
Solutions, dilute, 23.
Spallanzani, L., ix, 139, **155,** 163.
  Fisica animale, 155.
Specific nerve energies,
  Bell on, 252, 257, 258.
  Müller on, 274.
Spinal nerves, functions of, 261.
'Spiritus nitro-æreus', 111.
Spring and weight of the air (Boyle) 6, 107.
Standing reflex, 293.
Stanton, 302, 303.
Starling, E. H., **26,** 140, **178.**
Statical essays (Hales) 75.
Steno, N., 181.
Stepp, 300, 301.
Stokes's law, 17.
Stretch reflex, 288.
Struthers, J., 250.
Stuart, A., 181, 206, 207, 235.
Suprarenal capsules, 304.
Swammerdam, J., 18.
Sylvius, J., 52.
Sylvius (de la Böe), F., 139, 146.
Sympathetic nervous system, vasomotor nerves of, 281.

Tadinus, A., 146.
Telereceptors, 294.
Thermodynamics, history of, 18, 223.
Thomas, H. M., 289.
Thompson, 231.
Thomson, 87, 88.
Thunberg, T., 137.
Tiegs, 94.
Tractatus duo (Mayow) 111.
Tractatus quinque (Mayow) 112.
Transfusion, blood, 116.
Transfusion des Blutes (Scheel) 116.

Vagus inhibition, discovery of, 276.
Valves in veins, 41.
  Alberti on, 47.
  Fabricius on, 48.
  Galen on, 41.
  Harvey on, 50.
Vasomotor nerves, 281.
Vesalius, A., 106.
Veslingius, 160, 161.
Vimptrup, B., 94.
Vitalism, 32.
Vitamines, discovery of, 135, **299.**
Voit, C. von, **297.**
Volkman, A. F., 276.
Volta, A., 209.

Walker, A., viii, **247,** 250, 258.
Warrington, Academy, 119.
Water, function of, 34, 35.
Weber, E. F. and E. H., **276.**
Wedemeyer, 87, 88.
Wertheimer, 179, 180.
Whytt, R., 61, **79,** 235, **242,** 244 (portr:), 271.
  Physiological essays, 79, *Involuntary motions,* 242.

WILLIS, R., 44, 51.
WILLIS, T., 111, **192,** 194 (portr:), 195.
WILSON, 87.
WILSON-PHILIP, 276.
WOLF, C., 295.
WOTTON, W., 44.

X-rays, stomach and, 174.

YOUNG, J., 37.

ZOTTERMAN, Y., **232.**
ZUNTZ, N., 129, 133, 134.

THIS BOOK

SELECTED READINGS
IN THE HISTORY OF PHYSIOLOGY

was set, printed and bound by The Collegiate Press of Menasha, Wisconsin. The cover design is by The Decorative Designers of Chatham, New Jersey. The typographical design is by The Golden Hind Press of Madison, New Jersey. The type face is Garamont. The type is set 10 on 11 and 12 on 13 point Intertype. The type page is 27 x 45 picas. The end sheets are 25 x 38 - 80 White Antique Tuftex. The jacket is India Antique Buckeye (80 lb.). The text paper is 39 x 53 - 153 (70 lb. base) Ivory Polychrome. The binding is Holliston Waverly 301 T.

With THOMAS BOOKS careful attention is given to all details of manufacturing and design. It is the Publisher's desire to present books that are satisfactory as to their physical qualities and artistic possibilities and appropriate for their particular use. THOMAS BOOKS will be true to those laws of quality that assure a good name and good will.